THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—44TH YEAR SYDNEY, SATURDAY, JANUARY 19, 1957 No. 3

Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page.

The Effect of Food on the Absorption of Penicillin Given by Mouth, by E. R. H. Clarke, A. G. Mathews, Nancy D. Hesketh and M. G. Evered 61
Benactyzine Hydrochloride ("Suavitil") in Out-Patient Psychiatric Treatment: Preliminary Study, by R. Euan G. MacLean, M.B., B.S., D.P.M. 67
A Rural Tuberculosis Clinic in Korea: Summary of 160 Cases, by J. N. Burgess, M.B., B.S., D.D.R., M.F.R., M.C.R. 70
A Study of Stillbirths in the State of Victoria—1953, by F. M. C. Forster 72
Pneumonokoniosis in Victorian Industry, by D. L. Gordon Thomas 75
Remarks on Chronic Gastritis, with Special Reference to the Prevalent Inefficiency in the Examination of the Gastric Contents, by V. J. Kinsella 77
The Electrocardiogram of Racehorses: A Preliminary Communication, by J. D. Steel 78

REVIEWS—

Modern Gynæcology with Obstetrics for Nurses .. 79
A New Psychotherapy in Schizophrenia 79
Lectures on the Scientific Basis of Medicine 80
Proprioceptive Neuromuscular Facilitation 80

BOOKS RECEIVED 80

LEADING ARTICLES—

The College of Pathologists of Australia 81

CURRENT COMMENT—

Experimental Cardiopneumopexy 82
Linkage in Human Genetics 83
The Adrenal Gland and Experimental Cirrhosis of the Liver 83
Leuchæmia 84
Some Thoughts on Medical Education 85

CURRENT COMMENT—Continued. Page.

Clinica Chimica Acta 85
Two Healthy Development in Australian Medicine 85

ABSTRACTS FROM MEDICAL LITERATURE—

Therapeutics 86
Neurology and Psychiatry 87

BRITISH MEDICAL ASSOCIATION NEWS—

Scientific 88

OUT OF THE PAST 89

CORRESPONDENCE—

North Queensland Medical Conference, 1958 90
Active Immunization Against Tetanus 90
Nomenclature of the Blood Clotting Factors 90
Gout, Rheumatism and Infection from Hippocrates to Hench 90
Fat Embolism 91

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 91

POST-GRADUATE WORK—

School of Radiology at Royal Prince Alfred Hospital, Sydney 91

THE ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS—

The Adolph Basser Research Fellowship 92

DEATHS 92

DIARY FOR THE MONTH 92

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 92

EDITORIAL NOTICES 92

THE EFFECT OF FOOD ON THE ABSORPTION OF PENICILLIN GIVEN BY MOUTH.

By E. R. H. CLARKE, A. G. MATHEWS, NANCY D. HESKETH AND M. G. EVERED.

From the Commonwealth Serum Laboratories, Melbourne.

In text-books and reviews dealing with the oral administration of penicillin it is not uncommon to find recommendations that penicillin should be given before meals, or midway between meals. In most cases such statements are not supported by reference to any authority, and in other cases (Florey *et alii*, 1949; Hughes, 1950) references are given to experimental work—by McDermott *et alii* (1946) and by Stewart and May (1947), respectively—which seems to us to be inadequate support for advising against the giving of penicillin at meal-times.

We decided to study directly the effect on the duration of a therapeutic concentration of penicillin in the blood of giving the penicillin at seven different times in relation to breakfast, using the same 10 subjects for all the comparisons. The results indicated that consideration might well be given to administering penicillin orally at breakfast-time. A little over two years later, an opportunity came to confirm and extend these observations, in another group of 11 subjects given penicillin at six different times in relation to breakfast and lunch.

Experimental Investigation.

In the first series of experiments, 10 normal healthy adult volunteers were selected, care being taken to choose a group known (from preliminary experiments, in which penicillin was given after their normal breakfasts) to exhibit a wide range of serum levels. The 10 volunteers were divided into seven "groups" by arbitrarily pairing three couples. The experiment was conducted on seven different days, during a total period of eleven days. The dose of penicillin was arbitrarily chosen as 200,000 units of crystalline potassium penicillin G, administered as two tablets (containing also starch and sucrose), and swallowed with about 200 millilitres of cold water. The dose was given at seven different times in relation to a standard meal—namely, one hour and half an hour before the start of breakfast, in the middle of breakfast, and one, two, three and four hours after the start of breakfast. On each day of the experiment each group of volunteers received the dose of penicillin at a different time, in relation to breakfast, the assignment of dose-times to groups and days being in the form of a Latin square. The standard meal, which was eaten by each subject on each day of the experiment, consisted of cornflakes and milk, minced steak

and poached egg on buttered toast, buttered toast and marmalade, and coffee with milk and sugar. The quantities of the various dishes consumed by each person each day were closely similar. In every case the meal broke an overnight fast, and no more food was taken for at least four hours. Several of the subjects complained that the meal was a little too heavy for comfort.

Three samples of blood were withdrawn from each volunteer by venepuncture at various intervals after each dose of penicillin, and the serum separated from the samples was assayed against standard solutions of penicillin in normal human serum by a disk-plate diffusion method with the use of *Sarcina lutea* (strain 9341 of the American Type Culture Collection). The sampling times were chosen in an attempt to obtain from each subject, on each day, at least one sample of serum containing approximately 0·03 unit per millilitre in order to make the most reliable estimates of the persistence time of a therapeutic serum level.[1] No attempt was made to determine the peak concentration of penicillin in the serum, or to detect how soon after the dose penicillin appeared in the blood. Urine was also collected from each subject for at least four hours after each dose, and after appropriate dilution in phosphate buffer it was assayed by the cylinder-plate diffusion method with the use of *Staphylococcus aureus* (strain B313 of the Northern Regional Research Laboratories, Peoria).

In the second series of experiments, 12 normal healthy adult volunteers happened to be available. No preliminary experiments were made to determine their efficiency in absorbing penicillin. The 12 volunteers were divided at random into three groups of four subjects. The experiment was conducted on three consecutive days. The dose of penicillin was 100,000 units — smaller than in the first series, so that the morning dose would be less likely to interfere with the afternoon dose. Each dose was administered as a single tablet (similar to the tablets used in the first series) and swallowed with about 50 millilitres of cold water. The dose was given at three different times in relation to each of two standard meals—namely, one hour before the start of breakfast and one hour before lunch on the same day; in the middle of breakfast and the middle of lunch on another day; and one hour after the start of breakfast and one hour after lunch on the remaining day. On each day of the experiment each group of volunteers received the dose of penicillin at a different time, in relation to meals, the assignment of dose-times to groups and days being in the form of a Latin square. However, so few results were obtained from one volunteer (H.C.), because of difficulty experienced with venepuncture, that her rejection from the experiment seems warranted.

The standard breakfast, in this second series of experiments, consisted of cornflakes and milk, boiled egg and buttered toast, buttered toast and honey, and tea and sugar. No more food was taken for four hours, and after this interval each volunteer was given a standard lunch. This consisted of chicken noodle soup and dry toast, lean rump steak fried in fat, chipped potatoes fried in fat, raw tomato, tinned peaches and tinned reduced cream, and coffee with milk and sugar.

Blood and urine samples were collected and assayed as in the first series of experiments, care being taken by each volunteer to empty the bladder immediately before the second dose of penicillin each day. Also, in this second series of experiments, samples of whole blood were collected by capillary puncture before, and at short intervals after, the first dose given to each volunteer each day. These capillary blood samples were examined semi-quantitatively for the presence of penicillin, by a rough assay procedure with the use of *Sarcina lutea* plates, in order to check whether penicillin appears rapidly in the blood after oral dosage.

[1] In actual fact most of our sampling times were shorter than turned out to be desirable for this object. The sample potencies are clustered more closely around 0·05 unit per millilitre than around 0·03 unit per millilitre. For this reason, in the analysis of our results which follows, we have concerned ourselves with "persistence times of a 0·05 unit per millilitre serum level".

Results.

In Figures I to VII and VIII to XIII the individual volunteers may be identified by the shape of the symbols used. The hollow symbols represent the logarithms of the potencies of all the samples of serum found to contain not

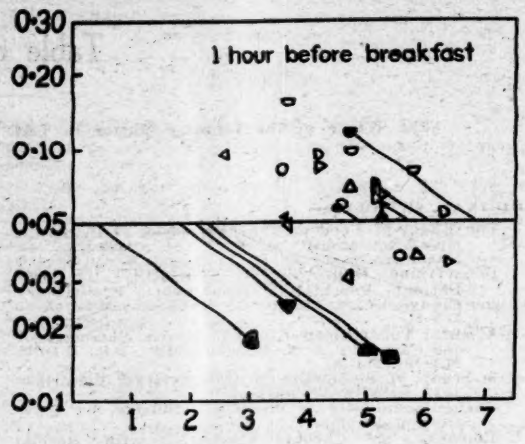

FIGURE I.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 200,000 units of potassium penicillin. The penicillin was given one hour before breakfast.

less than 0·025 unit of penicillin per millilitre, together with the corresponding time of sampling. Data in respect of samples containing less than 0·025 unit per millilitre have generally been rejected, on account of the unreli-

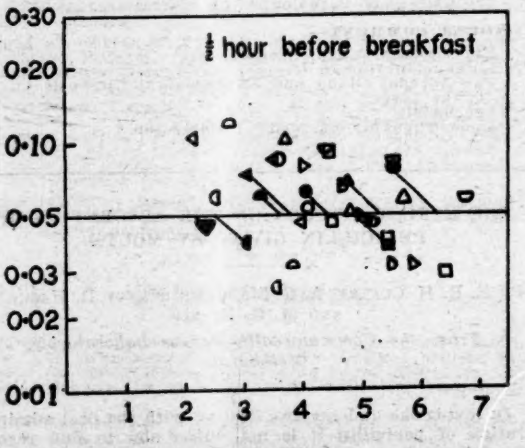

FIGURE II.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 200,000 units of potassium penicillin. The penicillin was given half an hour before breakfast.

ability of assay results in such weak solutions. However, if the three samples each contained less than 0·025 unit per millilitre, then the first such sample only is represented in Figures I to XIII.

The solid symbols in Figures I to XIII represent the means of the quantities represented by the corresponding hollow symbols in each figure. Through each solid symbol is drawn a straight line, of slope equal to the mean, for each figure, of the slopes of all the lines which could be

drawn to connect hollow symbols of the same shape. The point at which each of the lines shown intersects the horizontal line representing a potency of 0·05 unit per millilitre is taken as representing the "persistence time of a 0·05 unit per millilitre serum level" after each dose on each volunteer.

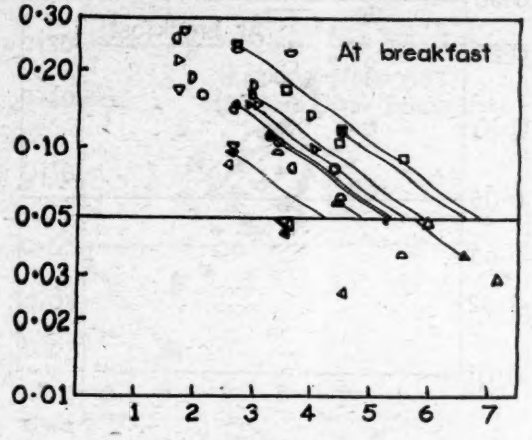

FIGURE III.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 200,000 units of potassium penicillin. The penicillin was given at breakfast.

This method of obtaining estimates of persistence time—indirectly, by way of average points and average slopes, rather than more directly by extrapolation of the lines of best fit which could have been drawn through the various sets of corresponding hollow symbols in Figures I to XIII—was adopted mainly to avoid the difficulties in estimating persistence times from those sets in which the apparent slope differs greatly from the average slope. Analysis of variance of the slopes found in individual sets showed that the variance between volunteers is not significantly different from the variance within volunteers, at the $P = 0·05$ level of probability, whereas the variance between dosage-time groups is significantly greater than the variance within dosage-time groups at the same probability level. These facts are some justification for drawing parallel lines of average slope in each figure.

For the first series of experiments the persistence times estimated from Figures I to VII are given in Table I, and in Table II is given the quantity of penicillin recovered in the urine of the volunteers after the various doses, expressed as a percentage of the dose administered. The corresponding results for the second series of experiments are given in Figures VIII to XIII and in Tables III and IV.

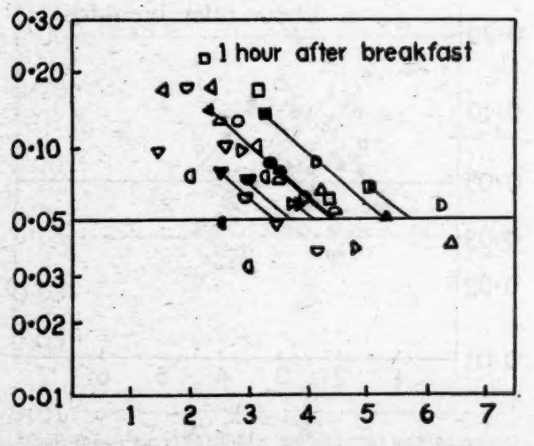

FIGURE IV.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 200,000 units of potassium penicillin. The penicillin was given one hour after breakfast.

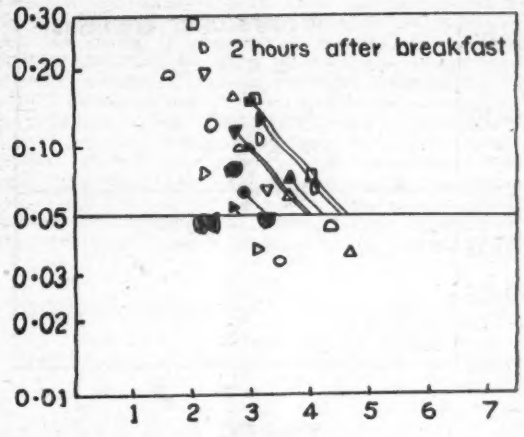

FIGURE V.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 200,000 units of potassium penicillin. The penicillin was given two hours after breakfast.

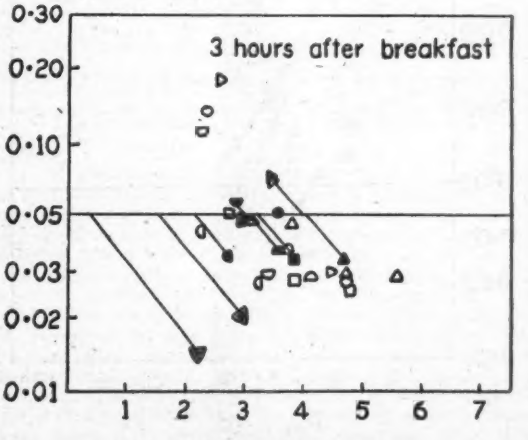

FIGURE VI.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 200,000 units of potassium penicillin. The penicillin was given three hours after breakfast.

Some data are given in Table V on the rate of appearance of penicillin in capillary blood. The times listed are those at which penicillin (*a*) appeared and (*b*) reached a concentration of 0·03 unit per millilitre (measured in whole blood) after the first dose on each day in the second series of experiments. This concentration of penicillin in whole blood was chosen for investigation because it is approximately equivalent to 0·05 unit per millilitre in serum.

In respect of the "before breakfast" dosage-time, concentrations of at least 0·03 unit per millilitre of whole blood were always found in the first sample, taken at an average of seventeen minutes after the dose. In the "at breakfast" case, penicillin could always be detected in the first sample taken after the dose, after an average interval of eighteen minutes. In most volunteers this sample contained at least 0·03 unit per millilitre of whole blood; in the others, this concentration was reached within thirty minutes of the dose. Absorption appeared to be somewhat slower still in the case of the "after breakfast" dosage-time.

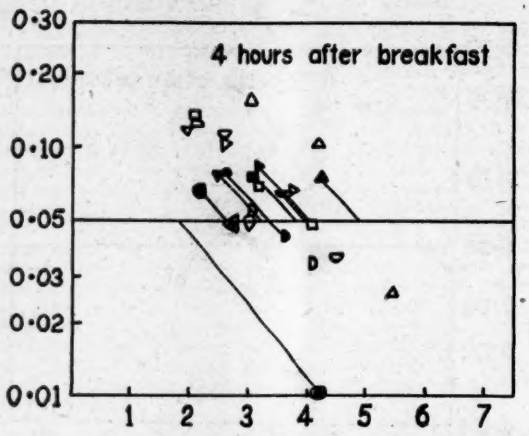

FIGURE VII.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 200,000 units of potassium penicillin. The penicillin was given four hours after breakfast.

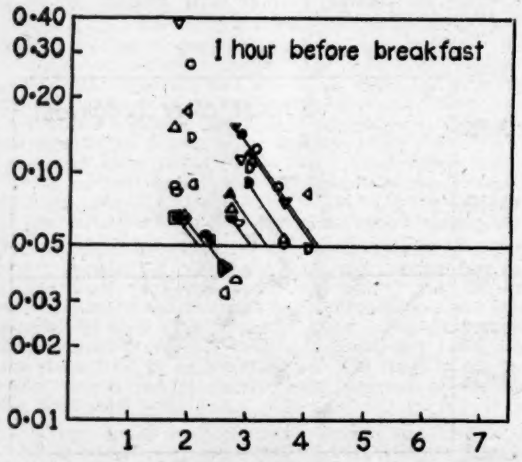

FIGURE VIII.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 100,000 units of potassium penicillin. The penicillin was given one hour before breakfast.

It will be seen from Figures I to VII and Table I that the median duration of a 0·05 unit per millilitre serum level, under the conditions of the first series of experiments, was greater when penicillin was administered by mouth in the middle of breakfast than when it was given either before or after the meal. The persistence time when the dose was given one hour before breakfast was about the same as when the dose was given one hour after breakfast. It will be noted that the persistence time decreased progressively for doses given one, two and three hours after breakfast, and increased only slightly when the dose was given four hours after breakfast.

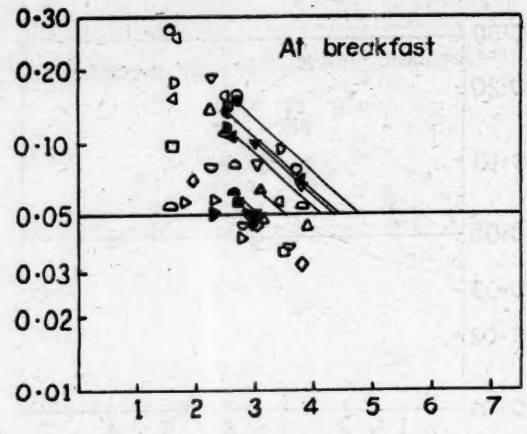

FIGURE IX.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 100,000 units of potassium penicillin. The penicillin was given at breakfast.

From Figures VIII to XIII and Table III it will be seen that under the conditions of the second series of experiments the longest persistence times were found when penicillin was given at breakfast, and the shortest when it was given one hour before lunch (which could also be expressed, in these experiments, as three hours after breakfast). In this series the persistence times for the one hour before breakfast dose were longer than those for the one hour after breakfast dose. Surprisingly, penicillin given one hour after lunch persisted for a slightly longer time than penicillin given during lunch.

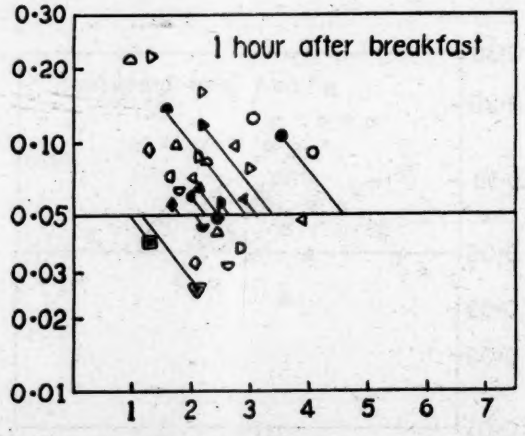

FIGURE X.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 100,000 units of potassium penicillin. The penicillin was given one hour after breakfast.

From the data on urinary recoveries of penicillin in Table II it will be seen that in the first series of experiments the quantities recovered in the urine were greater

after the doses given before breakfast, less after the doses given during breakfast, and still less after the doses given after breakfast. Table IV shows that the recoveries after the doses given at various times in relation to breakfast and lunch, in the second series of experiments, did not follow a simple pattern. However, the lowest recoveries were observed after the doses given between the meals.

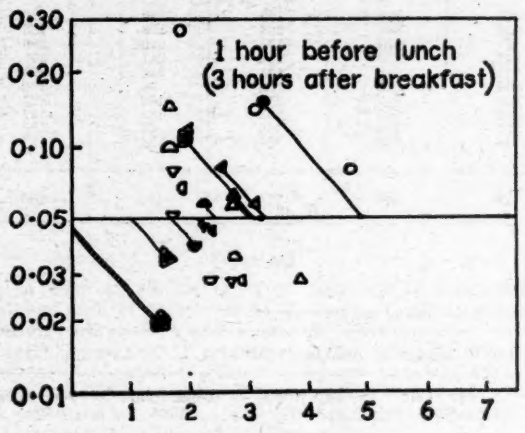

FIGURE XI.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 100,000 units of potassium penicillin. The penicillin was given one hour before lunch (three hours after breakfast).

The data in Table V show that penicillin appears very rapidly in the blood after oral administration, even when the dose is given with breakfast. Thus, the long persistence times observed after the oral administration of

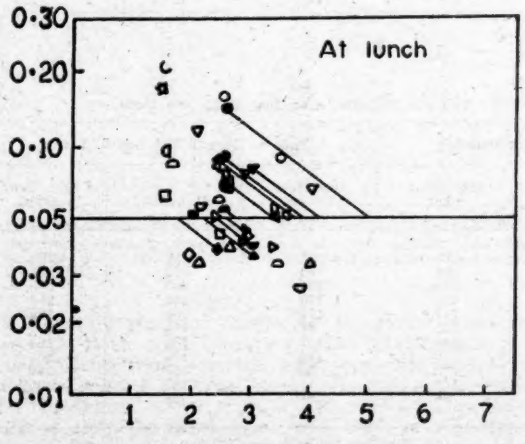

FIGURE XII.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 100,000 units of potassium penicillin. The penicillin was given at lunch.

penicillin with breakfast are not counteracted, as might otherwise have been postulated, by any long delay in absorption of the penicillin.

Discussion.

Many other workers, such as Young *et alii* (1952), have shown that penicillin is less well absorbed when given after a meal than when given before, as judged, usually, by the comparison of urinary recoveries or peak serum concentrations. From this work the conclusion has frequently been drawn, we think unjustifiably, that penicillin should not be given with a meal, but rather beforehand or midway between meals.

The experiments reported here show that the longest persistence of penicillin in the blood may be expected when the dose is given with meals. We have not been able to find any report of work which directly contradicts this finding. In fact, we know of only one comparison—by Stewart and May (1947)—of penicillin given with a meal, as well as before and after it. This work, although it led the authors to a conclusion unfavourable to the administration of penicillin with a meal, is not at variance with our results. Stewart and May used very small doses (15,000 units) and based their conclusions on a study of the highest concentrations observed in each subject for each dose-time in relation to breakfast. In most of their experiments no penicillin at all could be detected in the serum.

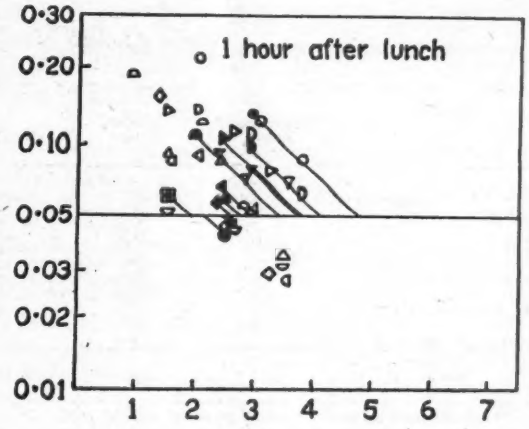

FIGURE XIII.

Concentrations (in units per millilitre) found in specimens of serum taken at various times (in hours) after oral administration of 100,000 units of potassium penicillin. The penicillin was given one hour after lunch.

In all our experiments we have directed our efforts towards estimating the duration of a therapeutic blood level and have made no attempt to detect the height or time of occurrence of peak serum concentrations. Whether penicillin given with a meal results in peak serum concentrations as high as those obtained after doses taken on an empty stomach thus remains an open question. The fact that, in the majority of the volunteers, less penicillin was recovered in the urine after the doses given with breakfast than after the doses given before breakfast, whereas the doses with breakfast resulted in longer blood-level durations than the before-breakfast doses, provides some indirect evidence that the absorption of penicillin is slower when it is given with breakfast than when it is given beforehand, and slow absorption would probably be associated, of course, with low peak concentrations. However, even if absorption of penicillin is slower when it is given with food, the data of Table V show that it is still fast enough to permit penicillin to be detected in the blood after a relatively short time.

With regard to the comparison of blood level persistence times following doses of penicillin given before and after meals, it is important to note that a dose given one hour after lunch was much better than a dose given one hour before lunch. On the other hand, our persistence time results in respect of doses given one hour after breakfast, in comparison with doses one hour before breakfast, were

TABLE I.

Time (in Minutes) Estimated for Serum Level of Penicillin to Fall to 0·05 Unit per Millilitre, After Dose of 200,000 Units.

Volunteer.	Sex.	Symbol.	Time of Dose in Relation to Breakfast.						
			One Hour Before.	Half an Hour Before.	At Breakfast.	One Hour After.	Two Hours After.	Three Hours After.	Four Hours After.
H.R.	Male.	▽	412	381	410	223	190	180	236
E.S.	Female.	▷	365	302	354	343	268	178	203
E.L.M.	Male.	△	345	300	337	248	170	240	236
E.C.	Male.	○	325	320	347	323	251	241	291
A.M.	Male.	◁	298	269	317	268	194	218	104[1]
F.T.	Male.	□	229	232	202	270	138	90	162
A.B.	Female.	▽	144	294	395	315	275	184	225
W.B.	Male.	▷	134	220	292	263	233	185	197
E.C.M.	Male.	△	114	133	253	209	236	12	187
C.McD.	Male.	◁	26	155	319	149	121	128	155
Median			264	282	328	266	214	182	200

[1] Suffered from indigestion between breakfast and the dose.

TABLE II.

Proportion of Penicillin Recovered in Urine, After Dose of 200,000 Units.

Volunteer.	Time of Dose in Relation to Breakfast.						
	One Hour Before.	Half an Before.	At Breakfast.	One Hour After.	Two Hours After.	Three Hours After.	Four Hours After.
H.R.	30%	21%	16%	3%	5%	7%	8%
E.S.	20%	19%	8%	12%	13%	7%	9%
E.L.M.	27%	17%	14%	5%	4%	9%	16%
E.C.	42%	22%	11%	No result.	12%	16%	28%
A.M.	22%	12%	12%	8%	6%	6%	3%[1]
F.T.	22%	15%	12%	10%	5%	5%	7%
A.B.	7%	20%	16%	14%	15%	9%	18%
W.B.	9%	22%	13%	15%	8%	3%	0·3%[2]
E.C.M.	16%	9%	8%	4%	8%	1%	15%
C.McD.	14%	11%	11%	2%	4%	3%	2%
Median	21%	18%	12%	8%	7%	7%	9%

[1] Suffered from indigestion between breakfast and the dose.

[2] Volume of urine passed was abnormally small.

TABLE III.

Time in Minutes Estimated for Serum Level of Penicillin to Fall to 0·05 Unit per Millilitre, After Dose of 100,000 Units.

Volunteer.	Sex.	Symbol.	Time of Dose in Relation to Breakfast.			Time of Dose in Relation to Lunch.		
			One Hour Before.	At Breakfast.	One Hour After.	One Hour Before.	At Lunch.	One Hour After.
R.F.	Female.	▽	255	264	74	125	249	223
J.H.	Female.	◁	250	257	188	193	232	184
R.B. ..	Male.	○	250	287	274	294	305	288
N.A. ..	Female.	▷	241	245	159	179	236	253
M.B. ..	Male.	△	204	212	147	179	132	168
I.V.	Female.	◁	187	177	125	98	145	130
I.H.	Female.	▽	151	269	134	127	205	150
E.M.	Female.	◁	146	181	173	146	164	203
M.B. ..	Female.	▷	141	140	210	59	158	229
K.L. ..	Male.	○	137	168	109	Nil	111	158
J.G.	Male.	□	132	175	58	Nil	127	114
Median			187	212	147	127	164	184

inconsistent, in that in the first series of experiments the doses one hour after breakfast and one hour before breakfast gave roughly equal persistence times, whereas in the second series the dose one hour after breakfast gave persistence times noticeably shorter than the dose one hour before breakfast. However, in both series doses of penicillin given two or three hours after breakfast clearly resulted in shorter persistence times than doses given before breakfast. Also, in both series, the amounts recovered in the urine were found to be less after the doses given one hour after breakfast than after the doses given at or before breakfast.

Closer examination of the results presented in Tables I and III shows that the serum-level-prolonging effect of a meal was more pronounced in those subjects who absorbed penicillin poorly when fasting. In effect, more uniform persistence times were observed when penicillin was given with a meal than when it was given beforehand.

TABLE IV.

Proportion of Penicillin Recovered in Urine, After Dose of 100,000 Units.

Volunteer.	Time of Dose in Relation to Breakfast.			Time of Dose in Relation to Lunch.		
	One Hour Before.	At Breakfast.	One Hour After.	One Hour Before.	At Lunch.	One Hour After.
E.F.	5%	13%	1%	6%	17%	10%
J.H.	21%	10%	5%	Nil.	9%	5%
E.B.	8%	No result.	6%	16%	No result.	7%
N.A.	27%	7%	8%	8%	15%	10%
M.E.	29%	10%	2%	27%	5%	12%
I.V.	9%	8%	7%	7%	8%	2%
I.H.	9%	11%	5%	1%	10%	5%
E.M.	7%	10%	5%	11%	10%	8%
M.B.	10%	10%	11%	9%	8%	9%
K.L.	10%	12%	6%	1%	6%	11%
J.G.	8%	12%	2%	1%	10%	4%
Median ..	9%	10%	5%	7%	10%	8%

Summary.

1. A dose of 200,000 units of penicillin G was given orally to each of 10 volunteers at seven different times in relation to breakfast, and a dose of 100,000 units to each of another group of 11 volunteers at six different times in relation to breakfast and lunch. The time required for the concentration of penicillin in the serum to fall to 0·05 unit per millilitre was estimated. The quantity of penicillin recovered in the urine was determined.

TABLE V.

Period (in Minutes) After First Dose (of 100,000 Units) Required for Penicillin (a) to Appear in the Blood, and (b) to Reach a Concentration of 0·03 Unit per Millilitre.

Volunteer.	Time of Dose in Relation to Breakfast.					
	One Hour Before.		At Breakfast.		One Hour After.	
	(a)	(b)	(a)	(b)	(a)	(b)
J.H.	<15	<15	<16	(x)	<18	<18
E.B.	<15	<15	<18	(x)	<20	<20
E.F.	<19	<19	<14	17	16–31	31
N.A.	<15	<15	<16	28	<20	<20
M.E.	<15	<15	<16	28	<18	<18
I.V.	<17	<17	<17	<17	(y)	(y)
I.H.	<15	<15	<16	<16	19–36	36
K.L.	(y)	(y)	<19	<19	<14	<14
J.G.	<25	<25	<25	<25	<14	21
M.B.	<16	<16	<16	<16	<14	<14
E.M.	<16	<16	<19	23	<15	<15

(x) Assay was partially spoilt, therefore no quantitative result is available.

(y) Penicillin was detected on the finger in a sample of capillary blood taken before the dose. Hence the results on subsequent capillary blood samples are invalid.

2. Penicillin persisted longest in the serum when the dose was given with breakfast. The next longest persistence times were observed when penicillin was given one hour or half an hour before breakfast or one hour after breakfast. The shortest persistence times were observed after the doses given two, three or four hours after breakfast. Penicillin given with lunch, or one hour after lunch, resulted in longer persistence times than the same dose given one hour before lunch (that is, three hours after breakfast).

3. Recovery of penicillin in the urine was usually greatest when penicillin was given before breakfast, less when it was given with breakfast, and least when it was given after breakfast. The time of administration in relation to lunch had little effect on urinary recoveries.

4. Penicillin can be detected in the blood almost as promptly after a dose given with breakfast as after a dose given on an empty stomach.

Acknowledgements.

Grateful appreciation is expressed to the volunteers—all members of the staff of the Commonwealth Serum Laboratories—who cheerfully took part in the experiments, and also to the staff of the Antibiotics Assay Department for the performance of the large number of assays required.

References.

FLOREY, H. W., CHAIN, E., HEATLEY, N. G., JENNINGS, M. A., SANDERS, A. G., ABRAHAM, E. P., and FLOREY, M. E. (1949), "Antibiotics", Oxford University Press, 2 : 1241.

HUGHES, W. H. (1950), "Methods of Administration", in "Penicillin", edited by A. Fleming, 2nd Edition, Butterworth, London : 114.

MCDERMOTT, W., BUNN, P. A., BENOIT, M., DUBOIS, R., and REYNOLDS, M. E. (1946), "The Absorption, Excretion and Destruction of Orally Administered Penicillin", *J. Clin. Investigation*, 25 : 190.

STEWART, H. C., and MAY, J. R. (1947), "Absorption of Penicillin Given by Mouth", *Lancet*, 2 : 857.

YOUNG, D. M., WILSON, R. J., and MACMORINE, H. M. G. (1952), "Oral Use of Penicillin G Ammonium", *Canadian J. Pub. Health*, 43 : 390.

BENACTYZINE HYDROCHLORIDE ("SUAVITIL") IN OUT-PATIENT PSYCHIATRIC TREATMENT: PRELIMINARY STUDY.

By R. EUAN G. MACLEAN, M.B., B.S., D.P.M.,
Psychiatrist Superintendent, Observatory Clinic, Melbourne.

ENCOURAGING reports from the Scandinavian countries, and the availability of a supply of "Suavitil" as well as matched inert control tablets (referred to as "placebo"), led to the initiation in February, 1956, of this controlled study of the effectiveness of the drug for out-patients in whom tension and anxiety were noted.

Benactyzine hydrochloride (the hydrochloride of 2-diethylaminoethyl benzilate) was known in Switzerland in 1936, but papers dealing with clinical trials (as "Suavitil" or "Parasan") seem not to have appeared until 1955.

Jacobsen, in Denmark, referred to the earlier known peripheral effects, benactyzine having an anticholinergic effect about a quarter that of atropine, a spasmolytic effect about half that of papaverine, and a quinidine-like effect on the heart about three times as great as that of quinidine itself, as well as a local anæsthetic action. He pointed out that the toxicity was low, and that in human subjects ingestion of four to six milligrammes was followed by dizziness, ataxia, and a feeling of relaxation in the voluntary muscles, together with a subjective feeling of blocking of spontaneous thought without hallucinosis, confusion or hypnotic effect. Objectively, the α waves disappeared from the electroencephalogram. In animal experiments small doses restored normal behaviour in artificially induced

TABLE I.[1]

Case Number.	Sex.	Age (Years).	Marital Status.	Diagnosis (Reaction Types).	Duration in Years.	Earlier Treatment.	Before Trial.		First Fortnight.				Second Fortnight.			
							T.	D.	S or P.	T.	D.	Clinical Judgement.	S or P.	T.	D.	Clinical Judgement.
1	M.	50	M.	Obsessive compulsive and psychosomatic	30	LCP	2	8	S	2	8	O	P	2	8	O
2	F.	49	M.	Obsessive compulsive with phobic features	12	CD	2	7	P	2	7	O	S	2	7	O
3	M.	28	M.	Anxiety hysteric with epileptoid features	8	E	1	4	P	1	4	O	S	0	2	B
4	F.	59	M.	Melancholic (cyclophrenia)	1 and 45	EC	2	9	P	2	9	O	S	3	9	A
5	F.	42	M.	Obsessional neurotic	28	C	2	7	P	1	4	A	S	0	1	B
6	F.	45	M.	Obsessive compulsive	17	C	2	9	S	1	6	B	P	2	8	A
7	M.	39	S.	Paranoiac	5	—	2	9	P	1	5	A	S	1	6	A
8	F.	27	M.	Obsessional compulsive with phobic features	1	C	1	10	S	2	12	W	P	1	8	A
9	F.	31	M.	Obsessional neurotic	5	—	2	8	S	2	6	O	P	2	5	B
10	F.	37	M.	Obsessional neurotic	20	—	2	6	P	1	4	A	S	0	3	B
11	M.	37	M.	Obsessional (latent psychosis)	5	—	1	6	S	1	6	O	P	1	6	O
12	M.	37	S	Obsessional neurotic	2	E	2	13	S	1	9	A	P	1	9	A
13	F.	34	M.	Anxiety hysteric with obsessional features	1·5	CP	2	9	S	1	6	A	P	1	6	A
14	M.	37	S.	Latent paranoid schizophrenic with obsessional features	1	C	2	9	P	2	9	O	S	1	4	B
15	M.	59	M.	Compulsion neurotic with latent psychosis	10 and 1	E	1	8	P	1	7	O	S	1	7	A
16	F.	36	M.	Obsessive compulsive	13	LEC	2	4	S	1	4	O	P	2	4	A
17	F.	39	M.	Anxiety hysteric with obsessional features	11	EC	2	7	S	3	10	W	P	2	6	O
18	M.	42	M.	Obsessive compulsive with hysterical features	25	C	2	7	P	2	7	W	S	3	8	X

[1] For explanation of abbreviations, see text.

stress situations, while conditioned responses were more frequent and coordinated. From this it was a short step to look on benactyzine as a potential chemical "tranquillizer" having a limited sedative action on the central nervous system, comparable perhaps with chlorpromazine and reserpine, but with slight side-effects only, and the blocking of the thought processes with elevation of the emotional threshold to external influences suggested an application to the neuroses.

Jensen, also in Denmark, had already treated with benactyzine 110 neurotic patients having an average age of forty years, improvement following in 75, of whom 56 became almost symptom-free, while in the control group receiving barbiturates the results were significantly poorer. Less rumination, greater accessibility to psychotherapy, relaxation, and "barriers" between the patients and their external worries seemed to appear, while the respite from externally induced worry could be used planfully, and realistic solutions could be felt possible.

Ostenfeld, at Velsted Mental Hospital, obtained encouraging but variable results in a trial with about 20 patients. In reviewing them he thought that in the patients selected the disease picture should be relatively simple, with the pathological processes mainly on an intellectual plane without dominating affective factors. Under those conditions he thought there was a good chance of being able to set a distance between a patient's disturbing disordered thoughts and his personality with a dosage of six milligrammes per day, sometimes rising to eight or nine milligrammes, but rarely more. He drew attention also to the combined use of benactyzine and amylobarbitone, the former influencing the formal thought processes and the latter giving affective calm.

Kehlet Munro, in a study of the effect of a daily dose of four milligrammes of benactyzine on eight healthy subjects, found that there was no effect on the ordinary intelligence functions, "but some highly organized functions, related to registration of a situation simultaneously with the attention to a task appeared somewhat impaired"; and the occurrence of subjective dizziness, heaviness of the limbs and slight thought block, together with disappearance of the α waves in the electroencephalogram, were confirmed.

Munkvad compared the effect obtained in some neurotic patients with that which lobotomy might have produced, but found that on the whole the psychoses were not influenced. With no risk of addiction, and no abstinence symptoms, treatment could continue in some cases for eight months or more, and the patients did not tend to increase their own dosage.

In England, Davies found that outside problems requiring the subject's attention created less tension and that the tension response tended to build up more slowly; while in his group of treated patients he found that a division could be made into two classes, irrespective of diagnosis —namely: (i) those who consciously or unconsciously wanted help and who derived some benefit provided that anxiety or agitation was present; (ii) those with a hostile attitude (overt, by projection, or via hysterical mechanisms) and who did badly, feeling the treatment to be inimical. It seemed that the hostile patient needed sharp contact with outer reality to be prepared for its surprises, or the enemies which might appear to be in it, resenting the characteristic divorce between that reality and emotional reactions produced by the drug. The author also considered benactyzine suitable for use in combination with other sedatives, particularly phenobarbitone, and sounded a note of caution concerning its use in the treatment of patients with phobic obsessional disorders or feelings of depersonalization or unreality.

Coady and Jewesbury concentrated on the possible effects of benactyzine in relieving muscular rigidity, spasm or pain in a group of 80 neurological patients, finding no effect on muscle tone and no significant relief of symptoms after two weeks on a dosage of six milligrammes per day, the subjective improvement reported by patients being similar to that obtained by the use of inert tablets. However, some patients reported relief from nocturnal flexor spasms.

Raymond and Lucas studied the effect of benactyzine in a series of 43 out-patients, finding that 12 of 18 patients in whom anxiety and tension predominated improved, and that those with depressive, hysterical and obsessive symptoms did not. Side-effects did not occur on a daily dosage of three milligrammes and were found in about half the patients receiving six milligrammes a day. While both Jensen and Munkvad had found that neurotic depressions were relieved, Raymond and Lucas could not confirm this,

and Jacobsen's explanation of the feeling of heaviness in the legs as being due to muscle relaxation was thought to be less correct than their view that it was due to a change in perception, for other perceptive changes occurred —for example, objects felt heavier, patterns for flicker were more coloured or intricate, and distances seemed altered. It seemed to them likely, then, that the substantial reduction in the quantity of α rhythm in the electroencephalograms of five patients was comparable to that following mescaline, in which the subject's attention to altered perceptions is thought to be an important factor.

TABLE II.

Case Number.	Rating at End of Trial.	Medication after Trial.	Rating at Each Stage.
3	B	2 weeks S (6·0 milligrammes daily).	B
4	A	1 week S (6·0 milligrammes daily).	A
		1 week S (4·0 milligrammes daily) with chlorpromazine (100 milligrammes daily).	B
		2 weeks S (3·0 milligrammes daily) with chlorpromazine (75 milligrammes daily)	B
		Further improvement on "Ritalin" and chlorpromazine.	
5	B	2 weeks S (6·0 milligrammes daily).	B+
		1 week without medication.	A
		3 weeks S (6·0 milligrammes daily).	O
6	A	2 weeks S (6·0 milligrammes daily).	O
7	A	2 weeks S (6·0 milligrammes daily).	A
		2 weeks without medication.	A
9	B	2 weeks S (6·0 milligrammes daily).	B
		1 week S (8·0 milligrammes daily).	A
		1 week without medication.	O
10	B	2 weeks S (8·0 milligrammes daily).	B
		6 weeks without medication.	B
13	A	1 week S (6·0 milligrammes daily).	B
		1 week S (8·0 milligrammes daily).	B
		2 weeks without medication.	B+
14	B	4 weeks S (4·0 milligrammes daily).	B+
15	A	1 week S (6·0 milligrammes daily).	A
		1 week placebo (8 daily).	A
		2 weeks without medication.	A
16	A	2 weeks S (6·0 milligrammes daily).	A+
		3 weeks without medication.	O
		1 week S (6·0 milligrammes daily). (To continue.)	A

Controlled Study.

Eighteen out-patients were selected for trial, all having some degree of anxiety and tension, and many ruminative activity. It was decided to keep to a standard oral dose of four milligrammes per day (two tablets twice daily), and to assign the patients at random to two treatments, those in group A receiving daily four tablets, each containing one milligramme of benactyzine, for fourteen days, while those in group B received four "placebo" tablets daily for fourteen days. The patients in each group changed to the opposite treatment after fourteen days and continued for fourteen days. The patients were unaware that two kinds of tablet were in use, while the psychiatrist did not know which patients were assigned to the two groups —that is, the "double blind" technique was used—and he did not know till the end of the trial whether a given patient was receiving drug or placebo during any given fortnight of the month of study.

During the trial no other drug or physical treatment was given, and psychotherapy was suspended.

A "rating of adjustment scale" was constructed, the psychiatrist rating each patient at the commencement and again after fourteen days and after twenty-eight days from it, the categories considered being tension/anxiety, emotionality, human relationships, reality testing, and level of functioning. In each case, weightings of 0 (normal) up to 3 could be given, so that the theoretical range was 0 to 15. Tension/anxiety scores have been noted in Table I (T), as well as the total disturbance score (D) at each rating (including T), so that in the eighth column appears the tension/anxiety score at commencement, in the ninth column the total disturbance score at that time, and similarly for T and D at the end of the first and second fortnights. While these ratings were made by a psychiatrist as objectively as possible, he also rated the patient at the end of each of the two fortnights in accordance with his opinion of the patient's whole well-being at these times on the following scale: O, unchanged; A, slight improvement; B, marked improvement; C, very marked improvement; W, worse; X, much worse. In some cases some apparent conflict may be noted between the two results, and preference has been given to the letter rating. The tenth and fourteenth columns indicate which kind of tablet was given in the corresponding fortnight (S, benactyzine; P, placebo), while the seventh column contains coded information concerning previous treatment, as follows: L, leucotomy; E, electroconvulsive therapy; P, phenobarbitone; C, chlorpromazine; D, "Drinamyl". Psychotherapy of various kinds had been given previously in all cases.

TABLE III.

Result.	Male.	Female.	Total.
Improved on S, but not on P ..	3	1	4
Improved on P, but not on S ..	0	2	2
Improved on P and on S to about an equal extent	2	1	3
Improved on both, but P more effective than S	0	0	0
Improved on both, but S more effective than P	0	3	3
Improved on neither P nor S ..	2	1	3
Worse on S, but not on P	0	2	2
Worse on P, but not on S	0	0	0
Worse on both P and S	1	0	1
Total	8	10	18

The average age of the eight male and ten female patients was forty-one years, the range being twenty-seven to fifty-nine years.

Psychological testing designed to measure tension level, perceptual organization, abstract reasoning and memory, concentration, and fantasy life, was carried out with all 18 patients at the commencement of treatment and again two weeks later. This material is being studied, and reference to it will appear in a later paper.

TABLE IV.

Diagnoses: Reaction Types.	Male.	Female.	Total.	Improved at End of Trial.
Obsessional	2	3	5	4
Obsessive compulsive	2	4	6	3
Compulsive, with latent psychosis	1	0	1	1
Anxiety hysteric	1	2	3	2
Latent paranoid schizophrenic ..	1	0	1	1
Paranoiac	1	0	1	1
Melancholic (cyclophrenia) ..	0	1	1	1
Total	8	10	18	13

Side effects were noted in five patients. Medication with known benactyzine tablets was continued after the trial whenever it was thought that the patient would be helped thereby, and the results are summarized below. The patient in Case 16 feels that she would not like to be without the drug, and here the comment of Sargant may be relevant—that when even a modified leucotomy is performed it may still take months for the symptoms to disperse gradually, and that since one can hardly expect the new tranquillizers to work more speedily than a leucotomy, we may be overlooking a group of chronic neurotics who need a tranquillizer for many months to allow the symptoms to abate. Benactyzine may be such a tranquillizer, and some of these patients on the trial may be of the kind that Sargant had in mind.

A statistical analysis of the improvements in the first and second fortnights, irrespective of treatment, based on the D ratings, seemed to indicate that improvements in the second period and non-improvements in the first were

larger than one would expect, the difference being significant at the 5% level of confidence ($\chi^2 = 4{\cdot}0$); and if the clinical judgement ratings are given arbitrary values (B = 5, A = 4, O = 3, W = 2, X = 1), one finds that in the nine cases in which placebo was given first the total of ratings while the placebo was being taken is 29 and the total while the drug was being taken is 36, whereas in the other nine cases the total while the drug was being taken is 29, and the total while the placebo was being taken is 34. Thus in the first fortnights the ratings are 29 and 29 (total 58), and in the second fortnights 36 and 34 (total 70); this seems again to indicate that time rather than choice of tablet is the important factor.

However, in the first period the choice is between having benactyzine and having inert tablets; while in the second period the choice is between benactyzine at the time and the after-glow of the benactyzine given in the previous fortnight; consequently it is probably not only the longer time which counts, although this is fairly certainly a factor, since the experiment is such that the careful arrangement of appointments at regular intervals and the concern of those cooperating in the trial could be expected to have a beneficial effect on neurotic patients.

Tables III and IV are of interest.

Summary.

A preliminary study of the effect of benactyzine on selected out-patients is presented. In this trial study of 18 patients, 13 were improved to a slight or moderate extent at the end of the trial period. However, in some cases return to the original state occurred within the next few weeks even when medication with the drug continued. While in some cases patients improved while taking inert tablets but not during medication with benactyzine, and while some improved on both to about an equal extent, none showed relatively greater improvement on inert tablets as compared with benactyzine. It will be seen from Table III that benactyzine could be said to have a moderate value in the treatment of patients selected as showing anxiety and tension. A controlled study in progress involving about 12 patients, all receiving six milligrammes of benactyzine daily, will be the subject of a further paper.

Acknowledgements.

The writer wishes to thank the Mental Hygiene Authority of Victoria for permission to publish this paper, and gratefully acknowledges the help given by Dr. Alan Stoller, Chief Clinical Officer of the Mental Hygiene Authority, Dr. G. L. Christie, Senior Medical Officer, Observatory Clinic (three of whose patients were included in this series), Mr. J. B. Lyle, psychologist, Mental Health Research Institute, and Mr. T. H. Esson, senior psychologist, Mrs. K. Ginter, psychologist, Sister B. Higgins, and the clerical staff of the Observatory Clinic. He is grateful also to Glaxo, Proprietary, Limited, for making available "Suavitil" and control tablets.

References.

COADY, A., and JEWESBURY, E. C. O. (1956), "A Clinical Trial of Benactyzine Hydrochloride ("Suavitil") as a Physical Relaxant", *Brit. M. J.*, 1: 485.

DAVIES, E. B. (1956), "A New Drug to Relieve Anxiety", *Brit. M. J.*, 1: 480.

JACOBSEN, E. (1955), "A New Drug Effective on the Central Nervous System", *Dan. Med. Bull.*, 2: 159.

JACOBSEN, E., KEHLET, H., LARSEN, V., MUNKVAD, I., and SKINHØJ, K. (1955), "The Autonomic Reaction of Psychoneurotics to a New Sedative: Benactyzine NFN, Suavitil (R)", *Acta psychiat. et neurol scandinav.*, 30: 607.

JENSEN, O. ØSTERGAARD (1955), "Suavitil in the Treatment of Psychoneuroses", *Dan. Med. Bull.*, 2: 140.

MUNKVAD, I. (1955), "Treatment of Psychoses and Psychoneuroses with a New Sedative (Suavitil)", *Acta psychiat. et neurol. scandinav.*, 30: 729.

MUNRO, H. K. (1955), "On the Effect of Suavitil on the Higher Mental Functions of Normal Subjects", *Acta psychiat. neurol. scandinav.*, 30: 74.

OSTENFELD, I. (1955), "A New Spasmolytic with an Apparent Action on Obsessive Compulsive and Related Disorders —Preliminary Report", *Nord. med.*, 54: 1523.

RAYMOND, M. J., and LUCAS, C. J. (1956), "Benactyzine in Psychoneurosis", *Brit. M. J.*, 1: 952.

SARGANT, W. (1956), "On Chemical Tranquillizers", *Brit. M. J.*, 1: 939.

A RURAL TUBERCULOSIS CLINIC IN KOREA: SUMMARY OF 160 CASES.

By J. N. BURGESS, M.B., B.S., D.D.R., M.F.R., M.C.R.,

Korea Church World Service, Seoul, Korea.

As part of the public health programme of a community coordinated development project in Sapkyo Myun, a tuberculosis out-patient clinic was commenced in April, 1955. This clinic is in a typical rural area about 100 miles south-west of Seoul, which has a population of about 20,000 people. There are two licensed Korean doctors in the district; one is a man aged about sixty years, who graduated from the Seoul National University, but has done very little reading since; the other is aged about forty years and has had no medical education, but he was an assistant to a Korean doctor for three years, and he passed a licensing examination six years ago. Neither of these men has any diagnostic acumen, and both are completely ignorant of the interpretation of X-ray films. Anyone with a chronic cough is considered tuberculous and is treated with streptomycin injections, so long as the patient can afford, or is willing, to pay for them.

The number of patients suffering from pulmonary tuberculosis in South Korea is estimated at about 1,500,000; about 500,000 of them need hospital treatment. There are only 5000 beds available in sanatoria and in the provincial hospitals. The Korea Church World Service, sponsored by the World Council of Churches and largely financed from the United States of America, started an out-patient chest clinic at Severance Hospital, Seoul, in 1954. There are now four chest clinics in Seoul and eight in the areas outside of Seoul. Now the Ministry of Health has established about 100 chest clinics throughout South Korea. These are provided with anti-tuberculosis drugs for a specified number of patients. Thus an extensive programme for treating tuberculous patients on an out-patient basis has been instituted. The Sapkyo clinic is an example of such a clinic in a rural community, and is under the auspices of the Korea Church World Service. The tuberculosis rate in this community is probably about 2%, making 400 patients in the district. However, many of the patients come from neighbouring areas and even from far distant places. The children in the Sapkya primary and middle schools were tested with tuberculin. The percentage of positive results in the primary school rose from 43 among the seven-year-olds to 60 among the twelve-year-olds, while in the middle school it rose from 70 at the age of thirteen years to 80 at the age of sixteen years. The average percentages were 50 in the primary school and 66 in the middle school. Those children who failed to react to the tuberculin test were given an injection of B.C.G. vaccine, while those who reacted were radiologically examined; but the radiological findings are not yet available.

The clinic has treated nearly 400 patients, of whom one-third are from Sapkyo. At present 325 are coming regularly for treatment, including 30 with joint tuberculosis. The nearest provincial hospital is at Hong Sang, 12 miles away; there the X-ray work for the clinic is done. Of the 325 patients, 160 have attended regularly for over three months, and have had repeated X-ray examinations and sputum tests. Those with joint lesions have not been included, though most of them have attended regularly. Joint tuberculosis seems fairly prevalent in the district, and none of the affected patients have had plaster casts or splints, so there are gross deformities and contractures. Many of the children with severe kyphosis have not been encouraged to walk, and so have shrunken legs. These have all been treated in the clinic with bi-weekly injections of streptomycin (0·5 gramme) and the oral administration of "INH" tablets (100 milligrammes). When the lesion is comparatively recent and the kyphosis is not too gross, then plaster jackets are applied. All the patients have been encouraged to move their legs and start walking. Those with involvement of the hip or knee have all been put

in plaster casts to prevent further deformities and contractures.

The clinic is under the supervision of an American public health nurse assisted by two Korean nurses and an interpreter, who also tests the sputum. The X-ray films are read fortnightly by an Australian radiologist, who also visits the clinic monthly. He examines the new patients after viewing their films, and then plans the course of treatment.

A summary of the findings relating to 160 patients who have been treated for three to fifteen months on an out-patient basis, with occasional visits from one of the nurses, makes available some interesting data. Of these patients, 72 have been treated for three to five months, 40 for six to eight months and 48 for nine to fourteen months. The basic treatment has consisted of the daily administration of 200 milligrammes of "INH" and 12 grammes of PAS; 107 patients are on this regime. "INH" alone in a dosage of 200 milligrammes per day was given to 46 patients; these included 13 with minimal and primary lesions, and 22 older persons with chronic disease of long standing. Only seven patients were treated with weekly injections of one gramme of streptomycin and the daily administration of 200 milligrammes of "INH". "INH" is used in all cases, and is given alone in minimal, primary and chronic disease. PAS is added in all other cases unless gastric disturbance is present. After three months a further X-ray examination is made, and if the film or the patient's condition shows deterioration, then streptomycin is substituted for PAS, and a similar re-evaluation is made again at six months. Streptomycin is allowed to be given in the clinic only by a trained nurse, and so PAS is considered the ideal supporting drug in an out-patient clinic. When the diagnosis is confirmed bacteriologically and radiologically, then the patient is given strict orders regarding rest, disinfection, and the prevention of infection. The nurse endeavours to visit the patient to assess home conditions. The other members of the household are asked to report for X-ray examination, and those aged under fourteen years are tuberculin tested. Those who fail to react are given B.C.G. inoculation, while those who do react are radiologically examined. The problem of adequate rest is a difficult one, as these people live in a rich farming district; the men have to help with planting, weeding and reaping the rice harvest, which is the main source of their income. The wives must also do the cooking, washing and cleaning, as no paid help is available. Thus the majority of the patients cannot rest completely, but they are encouraged to do so as much as possible. The economic position is also very worrying, as there is no regular income and the earnings are dependent on the capacity for work. There is no money for extra food or medicines, and so most adult patients suffer real hardship during their long period of illness. Drugs are given free, and powdered milk is handed out to the most needy patients.

The extent of the lesions assessed by X-ray examination in the 160 cases is as follows: far advanced, 93; moderately advanced, 50; minimal, seven; primary, six; miliary, four. It will be noted that 143 of the patients are classified as having moderately or far advanced disease; most of these have had symptoms extending over six months or more, and many have had previous treatment. The results of treatment as shown on the X-ray films are interesting. Improvement was found in 105 cases—slight in eight, moderate in 33 and pronounced in 64. Deterioration was found in only eight cases, and six of these patients had had less than eight months' treatment. In 48 cases no change had occurred; but 40 of these patients have had less than eight months' treatment. Thus 62% of patients have already improved, and it is probable that eventually 80% will show radiological improvement.

The sputum conversion rate is not so encouraging; in 22% of cases the finding changed from "positive" to "negative", though among patients who had had twelve to fourteen months' treatment there was a higher percentage —33. In only one case did the finding change from "negative" to "positive". This low rate of sputum conversion is primarily accounted for by the thoroughness of the person who makes the microscopic examinations, and does not indicate either the diminished number of bacteria on a slide or their degree of infectivity. No facilities have been available for testing drug-resistant organisms; these tests would be valuable, since many patients have received irregular treatment with anti-tuberculosis drugs. In all the cases in which the sputum findings are positive, the disease is far advanced.

With regard to the results of treatment, it is estimated that 15% of patients will need operation, 10 patients having atelectasis requiring lobectomy and 16 requiring pneumonectomy, while one patient has a broncho-pleural fistula. Thirty-six patients have discontinued treatment, 15 are classed as having the disease arrested, 11 as being cured (seven with minimal disease and four with miliary disease), five have chronic disease and will probably show no further improvement, and five require lung surgery.

Only one death has been reported; the patient was an undernourished girl with far advanced disease. The number of deaths due to tuberculosis in Korea is estimated at 400 per 100,000, or a total of 80,000 per year; this is tragically high.

Discussion.

These figures give an indication of the results of treating patients with tuberculosis on an out-patient basis with inadequate rest and insufficient diet; the results are nevertheless encouraging. It is considered worth while to continue such treatment in countries where sanatorium beds are few and the tuberculosis rate is high. The death rate can be reduced considerably, a small percentage of patients are cured, and the majority have their lesions controlled and their infectivity lowered. Tuberculin testing of school children is being carried out on a large scale, and those who fail to react are being given B.C.G. inoculation, which should make them partly immune to tuberculous infection.

A 150-bed chest hospital is being built and equipped by the United States Army. It is planned that it will be a centre where many lung operations will be performed, and also a post-graduate teaching centre for chest surgery, radiology and anæsthesia. A careful selection will have to be made of those to be operated on, out of the many hundreds who are suitable candidates for surgery.

It is realized that the majority of patients will have to continue taking "INH" indefinitely, with the hope that the disease can be controlled or that a more potent anti-tuberculosis drug will be discovered which will give them a chance of cure by medication.

Summary.

1. A tuberculosis clinic has been in operation since April, 1955, in Sapkyo Myun, a rural district about 100 miles south-west of Seoul, Korea, having a population of 20,000 people.

2. The tuberculosis rate in the district is about 2%; but two-thirds of the patients come from neighbouring districts.

3. The clinic has treated about 400 patients, including 30 with tuberculosis of joints; 325 are still under treatment, and 160 have attended for over three months.

4. Patients with joint and spine tuberculosis are put in plaster casts when possible and given bi-weekly injections of streptomycin and daily doses of "INH". The majority have chronic disease with deformities and contractures which are difficult to correct.

5. All patients with pulmonary tuberculosis receive 200 milligrammes of "INH" per day. Those with primary, minimal or chronic lesions receive "INH" alone; others receive in addition 12 grammes of PAS per day, except a few who receive one gramme of streptomycin bi-weekly.

6. Of the 160 cases, the disease is far advanced in 93, moderately advanced in 50, minimal in seven, primary in six and miliary in four.

7. In 105 cases improvement was shown on the X-ray film, and in 48 there was no radiological change.

8. *The sputum conversion rate was 22%, rising to 33%* in the cases in which treatment was of longer duration.

9. Of the patients, 15% are considered suitable for lung surgery.

10. Thirty-six patients discontinued treatment, in 15 cases the condition is classed as arrested and in 11 as cured, five patients have chronic disease, and one patient died.

A STUDY OF STILLBIRTHS IN THE STATE OF VICTORIA—1953.

By F. M. C. FORSTER,
Department of Obstetrics and Gynæcology, University of Melbourne.

IN 1952, legislation in the State of Victoria made it obligatory to provide certain relevant information concerning any stillbirth (Act Number 5623). In Victoria, a stillborn child is defined legally as follows:

> Any child born of its mother after the twenty-eighth week of pregnancy which did not at any time after being born breathe or show any other signs of life, and where the duration of pregnancy is not reliably ascertained includes any fœtus weighing not less than two pounds twelve ounces; and stillbirth has a corresponding interpretation.

Information concerning stillbirths is of medical and statistical interest and also of considerable social significance. The stillbirth rate is both an indication of the efficiency of obstetrical services and a reflection of the economic standards and general health of a community (Baird, 1947). It is important, therefore, that the recorded information, if it is to be of value, be as complete and accurate as possible.

This analysis presents part of the data made available by the Government Statist from the records of the Registrar of Births, Deaths and Marriages.

Incidence.

Eight hundred and seventeen stillbirths were registered in Victoria during 1953. Of these, 458 were reported in the Melbourne metropolitan area and 359 in the provincial centres and country. In the same year, the total number of live births in the State was 53,561, of which 27,560 were in Melbourne. The stillbirth rate for Victoria in 1953 was therefore 15 per thousand births, live and still. Stillbirths not registered because the period of gestation was unknown and facilities for weighing the baby were not available, probably constitute in Victoria an extremely small number. It is believed that a comparison between the stillbirth rate in Melbourne and that in the country would serve no useful purpose, because an unknown number of patients presenting obstetric difficulties are transferred from outlying centres to the metropolitan area.

Of the 817 stillborn infants, 425 were male and 377 were female. In 15 instances the sex was not recorded. Fœtal death occurred in 474 cases (59%) before labour and in 323 (41%) during labour. The time of death was not recorded in 20 instances. In over half (474 cases) the total stillbirths the period of gestation exceeded thirty-six weeks. In 161 cases it was thirty-two weeks or less, and in 30 it was not recorded.

Classification of Causes of Stillbirth.

In the analysis of the causes of stillbirth, the classification recommended by the World Health Organization (1948) has been adopted. This divides the causes of stillbirth into the following 10 main groups:

Group 1.—"Chronic Disease in Mother" (Y.30, World Health Organization classification) includes conditions such as cardio-vascular disease, chronic nephritis, *diabetes mellitus* and syphilis. These may have some effect on the fœtus although their ætiology is not related to the pregnancy.

Group 2.—"Acute Disease in Mother" (Y.31) is analogous to the previous group, and includes typhoid fever, influenza and pneumonia.

Group 3.—"Diseases and Conditions of Pregnancy and Childbirth" (Y.32) includes as the most important pre-eclampsia and eclampsia, and also includes pyelitis (pyelonephritis) of pregnancy and various thrombotic states.

Group 4.—"Absorption of Toxic Substance from Mother" (Y.33) refers primarily to the narcotic drugs and anæsthetic agents.

Group 5.—"Difficulties in Labour" (Y.34) includes prolonged labour, disproportion, fœtal malpresentations, abnormal uterine action, operative delivery, ruptured uterus, abnormality of organs or tissues of the pelvis and a number of other conditions.

Group 6.—"Other Causes in Mother" (Y.35) includes injury to the mother not due to the pregnancy.

Group 7.—"Placental and Cord Conditions" (Y.36) includes *placenta prævia*, premature separation of the placenta (accidental hæmorrhage), placental infarction and placental insufficiency, and various accidents to the umbilical cord.

Group 8.—"Birth Injury" (Y.37) to the fœtus excludes those cases in which there is a congenital malformation incompatible with life.

Group 9.—"Congenital Malformations of Fœtus" (Y.38).

Group 10.—"Diseases of Fœtus and Ill-defined Causes" (Y.39) includes hæmolytic disease (*erythroblastosis fœtalis*) and those cases in which there is no apparent cause for intrauterine fœtal death.

This essentially clinical and extremely detailed classification has been outlined to emphasize the necessity for exact recording of all knowledge regarding the cause of a stillbirth.

Analysis.

The causes of death in the 817 stillbirths reported in Victoria in 1953 are presented according to the World Health Organization classification (Table I). A more detailed analysis of the role of certain conditions is given (Table II).

Chronic diseases of the mother stated to have caused fœtal death were essential hypertension (eight cases), chronic nephritis (three cases), *diabetes mellitus* (two cases) and syphilis (one case). The acute maternal diseases were viral infections (four cases) and pneumonia (one case).

TABLE I.
Analysis of Causes of 817 Stillbirths, Victoria, 1953.

World Health Organisation Classification.		Number of Stillbirths.
Y.30:	Chronic disease in mother	14
Y.31:	Acute disease in mother	5
Y.32:	Diseases of pregnancy and childbirth	52
Y.33:	Absorption of toxic substances from mother	—
Y.34:	Difficulties in labour	71
Y.35:	Other causes in mother	2
Y.36:	Placental and cord conditions	279
Y.37:	Birth injury	12
Y.38:	Congenital malformations	70
Y.39:	Diseases of fœtus and ill-defined causes	312

Diseases of pregnancy and childbirth (52 cases) comprised 48 cases of pre-eclampsia and four of eclampsia. Twenty-four mothers were *primigravidæ*. There were five multiple pregnancies. In half the cases the period of gestation was greater than thirty-six weeks, and in one-third fœtal death occurred after the onset of labour.

There was no record of stillbirth due to absorption of toxic substances from the mother.

Difficulties in labour were reported to have resulted in 71 stillbirths. Thirty-eight of these were stated to be due to

prolonged or obstructed labour. This was reported more frequently from the provincial centres and the country (20 cases) than from the Melbourne metropolitan area (18 cases). Twenty-three additional stillbirths were attributed to difficulties arising from a labour in which the breech was the presenting part. In two-thirds of the latter cases the mother was a *primigravida*, and in nearly half the baby weighed more than seven pounds (3175 grammes). The remaining 10 stillbirths in this fifth group of the World Health Organization classification resulted from the following variety of causes: shoulder presentation (three cases), ruptured uterus (three cases, maternal shock (two cases), precipitate labour (one case), and maternal death (one case).

TABLE II.

Comparison of Specified Conditions Causing Stillbirth, Victoria, 1953.

Condition.	Number of Stillbirths.	Percentage Incidence.	Stillbirth Rate, by Cause, per 1000 Total Births.
General diseases of mother (acute and chronic) ..	19	2·3	0·4
Pre-eclampsia and eclampsia	52	6·4	1·0
Difficult labour (excluding breech presentation) ..	48	5·9	0·9
Difficult labour (breech presentation)	23	2·8	0·4
Accidental hæmorrhage ..	104	12·8	1·9
Placenta prævia	17	2·1	0·3
Prolapse of the cord ..	35	4·3	0·7
Fœtal malformations ..	70	8·6	1·3
Hæmolytic disease ..	42	5·1	0·8
Other defined causes ..	146	17·9	2·7
Ill-defined or unknown causes	261	31·9	4·6

Two stillbirths were attributed to injury to the mother. This resulted from a motor-car accident in both cases.

Placental infarction and placental insufficiency were recorded as causing 45 stillbirths. Thirty-five of these occurred before the onset of labour.

Fœtal death in 125 cases was ascribed to ante-partum hæmorrhage. There were 104 cases of accidental hæmorrhage, 17 of *placenta prævia*, and four which could not be classified. Accidental hæmorrhage was the commonest known cause of stillbirth in this analysis. It was recorded as a cause of fœtal death with almost equal frequency from the twenty-eighth to the fortieth week of gestation. Fœtal death in almost three-quarters of the cases (73 cases) occurred before the onset of labour.

Sixty-seven stillbirths were attributed to cord accidents such as entanglements, knots and torsion. In addition, 42 fœtal deaths were reported to have resulted from prolapse of the umbilical cord. In five instances prolapse of the cord occurred before the onset of labour.

Birth injury was recorded as being responsible for 12 stillbirths. Many such cases will almost certainly have been reported in the group of stillbirths resulting from difficult labour or delivery.

Seventy stillbirths were registered as due to recognizable congenital malformations. The commonest of these were anencephaly and hydrocephaly, of which there were respectively 31 and 15 cases. There were 13 stillbirths due to a variety of other abnormalities. In the remainder, the nature of the malformation was not stated.

In the final group, hæmolytic disease was reported to be responsible for 42 fœtal deaths. Ten of these were registered in the provincial centres and the country. There were nine other stillbirths stated to be due to diseases of the fœtus. In this last group are also included those cases in which the cause of fœtal death is ill defined or unknown. There were 261 stillbirths in this category. In 174 of these cases death occurred before the onset of labour, and in 164 the period of gestation was in excess of thirty-six weeks.

Discussion and Conclusions.

It is frequently impossible to compare information concerning stillbirths from various countries. This is due to differences in the definition of stillbirth. The World Health Organization Sub-Committee on the Definition of Stillbirth and Abortion, in an endeavour to obtain uniformity and wider knowledge of the problem of stillbirth, recommended in 1950 that the following definition be adopted by the member States:

> Fœtal death is death prior to the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy; the death is indicated by the fact that after such separation the fœtus does not breathe or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscle.

It was also recommended that the tabulation of all fœtal deaths was desirable, and that the following four groups should be used according to the duration of gestation calculated from the first day of the last menstrual period:

Group I: Less than 20 completed weeks of gestation.

Group II: 20 completed weeks of gestation but less than 28.

Group III: 28 completed weeks of gestation and over.

Group IV: Gestation period not classifiable in Groups I, II or III.

The definition of stillbirth as adopted in the State of Victoria thus corresponds with group III of the foregoing tabulation. It is obvious that the general acceptance of the completely inclusive interpretation of fœtal death, as formulated in this recommendation of the World Health Organization, would be of very great value. This is particularly true of the present time when increasing attention is being given to the influences of disturbances of early pregnancy.

A satisfactory classification of the causes of stillbirth presents many problems. The present confusion results from the different interests of obstetrician, pathologist and social worker. In this study a clinical approach has been adopted. The number of stillbirths in which the cause of death was substantiated by autopsy is not known, as the present form for registration of a stillbirth carries no inquiry as to whether a post-mortem examination was performed. It is considered that this information should be available.

A further criticism of the registration form is that it does not clearly define whether the period of gestation refers to the time when intrauterine death occurred or to when the fœtus was delivered. It is believed that knowledge of both figures is of value and that they should be reported when known.

Those stillbirths for which a variety of factors have been listed as being responsible present problems in assessment. They have been classified here according to what is considered the main cause. A further difficulty arises from individual differences of opinion concerning the significance of certain conditions causing fœtal death. Examples of these are placental infarction and placental insufficiency, which, in view of the present state of knowledge and subjective variations in their assessment, might equally well be placed with those stillbirths of which the cause was unknown (Morison, 1952).

It is believed that prematurity plays only a subsidiary role in causing fœtal death. In this survey, stillbirths reported as due solely to prematurity have been included in the ill-defined or unknown group.

Hæmolytic disease (*erythroblastosis fœtalis*) is responsible for a considerable number of stillbirths. In the World Health Organization classification it is grouped with other diseases of the fœtus, which are extremely few, and with those cases of fœtal death for which there is no apparent cause. This is unsatisfactory in view of the importance of this condition.

The incidence of ante-partum and intra-partum fœtal death in this study corresponded very closely with the findings of Dunham *et alii* (1938), who, in an investigation for the Children's Bureau (United States of America), reported that 58% of the fœtuses died before the onset of labour and 42% during labour. Intra-partum fœtal death in a large number of cases is due to mechanical difficulty in labour or delivery, and its incidence is some indication of the skill of the obstetrician and indirectly of obstetrical teaching.

It has not been possible to relate the social class, general physique and nutrition of the mother to the occurrence of stillbirth. This is a serious deficiency, for the importance of these factors has been amply demonstrated in recent years (Baird, 1947; Duncan, Baird and Thomson, 1952). They are an indication that the obstetrician must not concern himself solely with pregnancy. He must be vitally interested in the general health, economic status and way of life of the people in the community in which he is working. It follows, therefore, in view of this country's immigration policy, that details should be sought of the mother's country of origin and of the number of years during which she has been resident in Australia.

In the analysis of the causes of stillbirth, accidental hæmorrhage was the commonest known condition leading to fœtal death. This condition, until more is learnt of its ætiology, presents the greatest obstacle to any attempt at substantially reducing the stillbirth rate.

In half the cases of preeclampsia and eclampsia the period of gestation was greater than thirty-six weeks, and in one-third fœtal death occurred after the onset of labour. These findings suggest that some reduction in fœtal mortality in these conditions might be obtained by an increased awareness of their role in causing stillbirth.

In considering stillbirths due to dystocia, Marshall (1955) has made the following statement:

> No one has yet had the courage to state a figure for fœtal loss in relative disproportion and dystocia which an obstetrician or an institution can justifiably accept as reasonable and permissible. Of course the figure is zero and this is the ideal we strive for.

With particular regard to this group of stillbirths, it is believed that any study of the problems involved is incomplete without knowledge of the duration of labour and the method of delivery. These data are not at present available.

The number of stillbirths ascribed to entanglements, knots and torsion of the umbilical cord was surprisingly great. The significance of these conditions as causes of fœtal death is difficult to assess.

The disproportionately small number of stillbirths in the country reported as due to hæmolytic disease (*erythroblastosis fœtalis*) is at least in part accounted for by the transfer of many known Rh-immunized mothers for delivery in the specially equipped major metropolitan hospitals.

It is believed that the proportion of stillbirths (32%) placed in the group "cause ill-defined or unknown" may be reduced. In Scotland in 1939, the first year of a similar scheme of recording information concerning stillbirths, 32% of cases were also placed in this category. Douglas (1955) with reference to this has made the following statement:

> With the increasing interest taken by the medical profession this matter has gradually righted itself and this group has dropped to less than a third of what it was formerly.

In conclusion, it is stressed that a report such as this is dependent on detailed and accurate recording of information. This is illustrated by a study (Kohl, 1955) of perinatal mortality in New York City, carried out under the auspices of the New York Academy of Medicine, in which it was found that there was, with regard to stillbirths, only a 52% agreement between the diagnosis on the death certificate and that reached by the investigational subcommittee.

Recommendations.

There is at present in Victoria little direction to the medical practitioner as to the information concerning a stillbirth which should be reported. It is believed that a brief guide would be of assistance, and in this way more comprehensive data might be obtained. This guide could be attached to or incorporated in the form for registration of a stillbirth.

Attention has been drawn to a number of deficiencies in the information requested in the present registration form. It is considered that these should be corrected.

Finally, it is believed that consideration must be given to the practicability of adopting the definition of fœtal death, no matter what the period of gestation, which has been recently recommended by the World Health Organization.

Summary.

1. A study of stillbirths occurring in Victoria in 1953 is presented. This was the first year in which it became obligatory to provide certain relevant information concerning any stillbirth.

2. The number of stillbirths registered in that year was 817. The stillbirth rate was 15 per thousand total births.

3. The classification of the causes of stillbirth which was adopted in this report, that recommended by the World Health Organization, is outlined. The various difficulties encountered in an analysis based on this are discussed.

4. The causes of stillbirth are surveyed. Accidental hæmorrhage was the commonest of the known causes. The number of stillbirths for which the cause was ill defined or unknown comprised 32% of the total.

5. It is emphasized that the value of any study of stillbirths, such as the one presented, depends on full and accurate recording by the medical practitioner of all relevant information.

6. Attention has been drawn to a number of deficiencies in the present form for registration of a stillbirth.

7. It is recommended that a brief guide to what data are required should be attached to or incorporated in the registration form.

8. It is suggested that consideration be given to the practicability of adopting the definition of fœtal death which has been recommended by the World Health Organization (1950).

Acknowledgement.

I wish to express my appreciation of the help in the preparation of this report given by members of the Department of the Government Statist. In particular, I desire to thank Mr. G. E. Kitson.

References.

BAIRD, D. (1947), "Social Class and Fœtal Mortality", *Lancet*, 2: 531.

DOUGLAS, C. A. (1955), "Trends in the Risks of Child-Bearing and in the Mortalities of Infants during the Last 30 Years", *J. Obst. & Gynæc. Brit. Emp.*, 62: 216.

DUNCAN, E. H. L., BAIRD, D., and THOMSON, A. M. (1952), "The Causes and Prevention of Stillbirths and First Week Deaths", *J. Obst. & Gynæc. Brit. Emp.*, 59: 183.

DUNHAM, E. C., TANDY, E. C., DAILY, E. F., and HAYES, C. E. (1938), "Problem of Causes of Stillbirth", *Am. J. Pub. Health*, 28: 491.

KOHL, S. G. (1955), "Perinatal Mortality in New York City", Harvard University Press, 84.

MARSHALL, C. M. (1955), in "British Obstetric and Gynæcological Practice. Obstetrics", edited by Holland, E., Heinemann, London: 985.

MORISON, J. E. (1952), "Fœtal and Neonatal Pathology", Butterworth, London: 97.

WORLD HEALTH ORGANIZATION (1948), "Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death", Sixth Revision. World Health Organization, Geneva.

PNEUMONOKONIOSIS IN VICTORIAN INDUSTRY.

By D. L. GORDON THOMAS,
Industrial Hygiene Division, Victorian State Health Department, Melbourne.

SINCE the end of World War II Australia has been undergoing rapid industrial expansion in all fields, coupled with large-scale immigration. Although in 1956 some 43% of the national income comes from wool, the situation in the years to come may well be different. In view of the ravages to health which such industrialization has produced in the past in other countries, it was considered essential to obtain some facts on what had happened in Victorian industry in the immediate past in terms of industrial chest diseases. Without accurate knowledge of where the hazards really lie, it is impossible to have industrial expansion without a health toll. Without this knowledge there can be no planning for the future, and the mere policing of regulations leaves much to be desired in the field of preventive medicine. Accordingly, in 1952 a survey to determine the sources and incidence of pneumonokoniosis was commenced by the Industrial Hygiene Division, and the various aspects of the findings are now presented.

The total number of cases reported to the division prior to the survey was 522, which included 343 among miners and 179 industrial cases. The figures now read as follows: total 1126, with 587 in miners and 539 in industry. The X-ray investigations were carried out on full size film (17 inches by 14 inches) on personnel who in the opinion of the division were employed in dusty trades. The total number of individuals radiologically examined was 3823. Table I shows the results of the investigation.

In the survey, the number of moulders radiologically examined was 1918, and the percentage affected was 4·6. Three hundred asbestos workers were examined and this number would cover most of those exposed to dangerous amounts of dry asbestos dust; here the percentage was 15.

The most dangerous occupation is mineral grinding, largely of quartz, and here 30% of those radiologically examined were affected. In the other categories the people surveyed were those exposed to the greatest risks in the particular occupation, and not the employees as a whole, so that any computation as to the percentage affected in those industries would be erroneous. In the 360 cases found, all the subjects have been examined, their industrial histories have been taken and their exposure to dust has been confirmed. Apart from those suffering from asbestosis, the great majority are silicotics, many of whom are grossly disabled and many short of breath; others appear to be quite well apart from a slowing up and slight shortness of breath, and some are entirely symptomless.

Discussion.

Silicosis.

If we consider the conditions in the various types of occupation we find the following factors:

1. Moulders are exposed to silica in the moulding sand and often in the parting powder. One of the cleanest foundries investigated produced the highest proportion of silicotics (10%), owing to the fact that they were using silica flour, which is very finely ground quartz, as a parting powder. Many moulders with long exposure are grossly disabled.

2. Dressers are exposed to moulding sand and to fine metallic particles produced when castings are cleaned by emery wheels, automatic chisels and swing grinders. The tools in general use are now power-driven, and recently methods of exhausting the actual tool are being evolved. Some of these men have gross X-ray changes which are out of all proportion to their symptoms, while others with less pronounced changes are gravely affected. In cases in which the bulk of the inhaled dust is metal, the symptoms are usually slight.

3. Brick, tile and pottery workers are exposed to silica, and conditions in these occupations are particularly hazardous, inasmuch as the silica-containing substances are newly ground. The highest incidence was in a tile (wall) works, where flint was used in considerable quantity.

4. Mineral earth workers are the most exposed of all. Quartz, diatomaceous earth and asbestos are ground with usually makeshift machinery, and the dust hazard is extremely bad. One subject, a man aged thirty-five years, died of uncomplicated silicosis within nine years of commencing employment. These places have an unenviable record of death and disablement.

5. Masons and quarrymen are exposed to the dusts of various types of stone. Granite can contain up to 30% of free silica, and Stawell stone and Sydney freestone are for all practical purposes pure sand. Basalt quarrymen can develop an X-ray picture which is hard to distinguish from silicosis, but these men are free from symptoms.

6. Boilermakers and welders are exposed to mixed dusts. Few in this group are incapacitated.

7. Metal polishers are subjected to silica dust through the abrasive they use, which is beeswax impregnated with pure silica and known to the trade as "tripoli".

8. Stokers are exposed mainly to coal dust.

TABLE I.

Subjects' Occupations.	Number Radiologically Examined.	Number of Cases of Pneumonokoniosis Found.	Percentage of Positive Findings.
Moulders	1918	91	4·6
Brick, tile and pottery workers	388	51	—
Dressers	214	31	—
Mineral earth workers	41	14	30·0
Masons and quarrymen	171	26	—
Boilermakers	130	23	—
Metal polishers	203	38	—
Asbestos workers	300	47	15·0
Spray painters	20	7	—
Cleaners	8	2	—
Food workers	25	4	—
Rubber workers	47	9	—
Wood grinders	12	2	—
Cinematograph operators	17	4	—
Dry cleaners	4	1	—
Stokers	34	10	—
Foundry labourers	—	—	—
Plaster workers	—	—	—
Cement workers	291	—	—
Odd occupations	—	—	—
Bricklayers	—	—	—
Road workers	—	—	—
Total	3823	360	—

9. Rubber workers are exposed to talc, which is magnesium silicate; this can produce similar effects to silica and a similar radiological picture.

10. Cinema operators are exposed to carbon, metallic oxides, fluorides and silica from the carbon arc lights used in the machines.

11. A chance X-ray picture of a worker in a dry-cleaning establishment showed nodulation with no symptoms. Investigation showed that diatomaceous earth is used in the process of dry cleaning and constitutes a hazard. A survey of this industry is under way.

The radiological appearance must not be used as a yardstick to measure the severity or otherwise of the disease. Some subjects with gross X-ray changes are almost symptomless, while others who are gravely disabled show very little abnormality.

In the survey there are several sets of brothers who both developed silicosis in entirely different occupations. This suggests a familial tendency. One family group of seven boasts six silicotics affected in three different processes.

A person quite unaware that he is suffering from silicosis can, after an acute pulmonary episode, become totally disabled in a very short time. There are at least 20 listed who have graduated from the "mild short of breath" class to the "totally disabled" in periods in all cases less than four years. The use of 35 millimetre film is generally unsatisfactory in the diagnosis of pneumonokoniosis. Many cases, especially early ones, are missed. This could explain the great number of silicotics who are under treatment for dyspnœa, who have misled their doctors unwittingly by saying that in the mass X-ray examinations their chest findings were clear. The X-ray appearances can return to normal after the subject's removal from exposure to some dusts. This has occurred with wood dust, powdered food, starch and metal. Very few cases reported in this survey are complicated by tuberculosis. However, several cases have been reported from sanatoria, in which exposure to dust has been proved and compensation obtained. No cases of carcinoma of the lungs were found.

Both silicosis and asbestosis are so insidious in their progress and so easily influenced by acute pulmonary conditions that it would appear wise to advise the subject to seek a new occupation away from the hazard when shortness of breath becomes apparent, irrespective of his age. The following case illustrates this:

In 1952 a moulder of twenty years' standing was found to have typical silicotic X-ray appearances with nodulation and mild symptoms. He was earning big money and did not feel disposed to give up his job. In 1953 he had influenza with pulmonary complications, and today he is completely incapacitated.

The fact that pathological changes can continue in the lungs long after removal from the hazard must also be realized.

A woman, now aged thirty-nine years, was employed in a pottery plant. She worked there from the age of fourteen years until she was twenty-one, when she married. She had three children and carried on quite happily until five years ago, when she began to be short of breath, and an X-ray examination revealed abnormality. Her condition was eventually diagnosed as silicosis after tentative diagnoses of tuberculosis and sarcoidosis were disproved.

An inadequate industrial history delayed the correct diagnosis in this case.

There are two interesting subjects who served in the Western Desert with the Royal Australian Air Force during the last war. They were mechanics in fixed camps and their X-ray findings are typically silicotic. It would appear that they developed the condition on service. Heavy transports and tankers probably ground the sand to powder fineness, and the propellers these men used to swing produced an intensely heavy cloud of pure silica.

Many incapacitated men could cope with a sedentary job if it were not for the effort of travelling to and from work. In view of the progressive nature of the disease and the limited sum payable as compensation, we advise affected people to remain at work as long as possible—out of the hazard, of course. The ability to continue in useful employment is often increased by a course of physiotherapy.

Asbestosis.

In the section of the survey relating to asbestos workers, 300 men were examined; 100 had sputum containing asbestosis bodies, and of this 100, 47 had positive X-ray findings. In this last group all had symptoms ranging from shortness of breath on exertion to gross incapacity.

The procedure adopted was as follows: Specimens of sputum were taken and examined for the presence of bodies. When these were demonstrated, the patient was radiologically examined. When both tests gave positive results the patient was interviewed, a complete industrial history was taken and his clinical condition was assessed. If he had symptoms referable to the disease a diagnosis of asbestosis was made and the patient was advised to apply to the Workers' Compensation Commission for acceptance of his disability. Subsequently practically all workers exposed to dry asbestos have been radiologically examined.

The following occupations are involved: handling the substance in its raw state; grinding the substance prior to its use in some process; mixing with diatomaceous earth or kaolin to form lagging materials; sawing, cutting and finishing any product containing asbestos—for example, brake linings, asbestos sheeting and various insulating materials; tearing down old lagging—this is a very dangerous process, even in the open air; spraying asbestos on walls and ceilings as an insulator.

The pulmonary fibrosis of asbestos workers is insidious in its onset, irregular in its course, and variable in its termination; but once established it constitutes a grave threat to life and health. Briefly the pathological changes are such that the air cells become obliterated by fibrous tissue. As this progresses the lung tissue becomes used up and the elasticity of the lung deteriorates, the amount of lung available to carry out functions diminishes and symptoms appear. The condition is progressive and irreversible, and once the stigmata appear the subject should be removed from the hazard. The main symptom is steadily increasing shortness of breath. While there is no evidence that asbestosis predisposes the subject to acute pulmonary infections, the presence of the condition seriously impairs the chances of recovery when infection does occur. The advent of the sulphonamide drugs and of the antibiotics has greatly improved the prognosis in these cases.

The most sought after asbestos in industry is the type with long needles, but unfortunately this is the most hazardous type to handle. The needles enter the lung by inhalation, and after a time undergo changes in appearance and are then known as asbestosis bodies. They are brown or yellow in colour and are found in no other condition. The bodies are all modifications of a straight fibre and are shaped like dumb-bells, a drum major's baton, and so on. It is impossible to state at what period these appear, but they have been found in this survey as early as fifteen months after exposure commenced. The presence of these bodies must not be regarded as diagnostic of asbestosis, but it is conclusive proof that the patient has been exposed and that some abnormal process is at work in the lungs.

Unlike silicosis, the radiological findings in asbestosis are in accord with the severity of the symptoms. The greater the incapacity, the more one expects to see in the X-ray film. In the well-developed case the bases of the lungs, more especially the right, show a ground-glass appearance, and the outline of the heart is irregular or "shaggy". It is fully realized that a radiological diagnosis of early asbestosis is extremely difficult, and our cases were regarded as such only after the most careful consideration. A few films picked out at random were sent to England for review, none of them being from well-developed cases. One case was accepted as asbestosis on English standards. In the others, while it was admitted there were increased markings at the lung bases, the viewer stated that he had seen many similar films in his area from people who had never been exposed to asbestos. However, as these films were taken in a highly industrialized area where fog, soot and smoke abound, it is thought that to compare these with films of Australians of the same age proved nothing. Criticism will no doubt be directed at the standards of diagnosis; but if one waits until the stigmata of a well-developed case appear, one can do little for the patient.

It does not follow that everyone is going to accept the advice tendered to leave the hazard; but since the number of workers in this group is comparatively small, the realization that their friend who was supposed to have a weak heart for a long time is actually suffering from asbestosis and is eligible for compensation is making most workers very conscious of the hazard. Much more care has been exercised by the workers in recent times, and they are much more easily persuaded to wear a mask.

The most common symptom is shortness of breath on exertion. Tightness in the chest and pain in the chest are not uncommon, with lack of energy and tiredness. Most patients show an improvement after a course of physiotherapy. The patients given a course of physiotherapy had all been accepted for compensation, and all were kept in hospital for at least a month, so that the rest and elimination of worry for the future were also beneficial

factors. All those given this course are still working at light sedentary occupations. When this survey started, eight cases of asbestosis had been reported and the disease was regarded as a rarity. It will be seen from the figures that the incidence of the disease is far too high. In addition to those found in the investigation, there must be many more older folk suffering from the complaint in whom it has not been diagnosed, and who are incapacitated and very poorly off financially, and should be receiving adequate compensation.

Summary.

Three hundred and sixty cases of pneumonokoniosis were found in industry in Victoria. No doubt there are many more, either symptomless or undiagnosed.

Silicosis and asbestosis are not diseases of the aged. Many of these subjects belong to the thirty to fifty years age group, and for this reason it is imperative that conditions improve in the dusty trades. The two conditions can occur together, causing gross disability. Six affected persons, who showed nodulation and also asbestosis bodies, were found in the same factory. They are very disabled, and two are aged under forty years.

The survey illustrates the necessity of impressing on medical practitioners the need for taking a complete industrial history of all patients irrespective of sex. It is not sufficient to ask a person his or her occupation—a bread carter today may have been a miner twenty years ago. Many women have worked and are still working, although the hazards now are less damaging.

Industry in Victoria is becoming very dust-conscious. While these investigations have been proceeding, the Industrial Hygiene Division has been busy encouraging the suppression of dust. Unions have sponsored the survey and employers have been most cooperative in allowing their personnel to be radiologically examined in the firm's time. In the firms where cases have been found, close inspections have been made, and where possible conditions have been improved by exhaust ventilation, by better housekeeping, or by the elimination of the hazardous substance. The use of respiratory devices is recommended only when the hazard is of short duration and when other methods cannot be used effectively. Conditions in industry can be greatly improved in many cases by very simple means—even damping down the floors in a foundry led to big reductions in dust counts.

Legislation has been introduced to try to improve conditions. Quartz grinding has been declared a dangerous trade. This means that any premises used for the process must be registered, and in the event of the regulations not being complied with the registration can be withdrawn and the firm becomes liable if it continues to work in an unregistered building.

Asbestos regulations are awaiting gazettal. These are very stringent, and when in force will lead to a big improvement in conditions. However, the most important single factor is to educate the worker to protect himself. Many, many times one can see expensive, most effective exhaust apparatus rendered useless by some worker who "didn't like the draught" pushing a bag up a duct or some other equally silly practice.

When one has seen the end results of these two dust diseases—the gross incapacity, the patients' realization that the steady deterioration is inevitable, and in many cases the financial difficulties due to their having used up the compensation paid—it becomes imperative to ensure that as industry expands, industrial hygiene matches the expansion stride for stride.

Acknowledgements.

My thanks are due to Dr. Keith Hallam for his invaluable help on the radiological side, and to Dr. D. O. Shiels for our many discussions on dust problems.

REMARKS ON CHRONIC GASTRITIS, WITH SPECIAL REFERENCE TO THE PREVALENT INEFFICIENCY IN THE EXAMINATION OF THE GASTRIC CONTENTS.

By V. J. KINSELLA,

From the Department of Gastro-Enterology, Saint Vincent's Hospital, Sydney.

WHEN a hollow organ is afflicted by disease, a proper understanding of the processes at work is helped considerably by a study of the discharges provoked by the disease. The discharges are in fact a sign of the disease in the walls. Diagnosis and treatment would lose considerably if this element were neglected. Thus, the nasal and post-nasal discharges, the sputum pot, the urinary testing glass and the contents of the bed pan provide the clinician with valuable information, which helps to truth in diagnosis and to success in treatment. Moreover, an increase or decrease in these discharges, or a change in their quality, provides valuable evidence of the progress of treatment.

But the stomach is unique. When it is stricken, its tears are often ignored; the nature of its disease is thus unrecognized, a faulty prognosis is given, and inept treatment is ordered.

For this, several factors are responsible. One is the neglectful reports on the gastric contents made by pathologists and biochemists. A few years ago I asked a senior teaching biochemist why he gave no report about mucus in fractional test meals. He gave as the reason that the mucus could come either from the respiratory tract or from the stomach, and that therefore its significance could not be interpreted.

It is, of course, highly unscientific to suppress evidence merely because its interpretation is difficult. Moreover, there is always the chance that somebody else may succeed in the interpretation. Thus, by examining the respiratory tract, the clinician may get a very good idea as to whether it is the source of the discharge. But even the biochemist, if properly instructed in his art, should be able to make the distinction easily.

If the excess mucus is gastric in origin, it appears in each specimen. It is intimately mixed with the gastric contents, so that, when the contents are poured from one test-tube to another, they are seen to be more viscous. The mucus is finely flocculated. An approximate quantitative account of this mucus can be given in terms of filtration time.

Mucus from the respiratory tract occurs chiefly in the fasting gastric contents, it is in larger discrete masses, it often includes air bubbles, it is easily seen when pressed out under a cover-slip, and it floats on the surface of the gastric contents. The discovery of such mucus or mucopus may give a valuable therapeutic hint to the clinician.

The fasting gastric contents should then be examined microscopically. Gastric mucus contains the nuclei of leucocytes whose cytoplasm has been digested, staining deeply with methylene blue, and columnar or goblet cells. In gastritis, there may be large numbers of granular cells (these are desquamated glandular cells) or a persistent increase in leucocytes. In cancer one may find polygonal, round or cylindrical cells, with characteristic volume, density and multiplicity of nuclei. Eosinophile cells may give the clue to an allergy.

Naso-pharyngeal mucus may contain squamous epithelial cells and carbon particles.

Note should also be made of the bacterial population. It is increased in hypochlorhydric gastritis and in cancer.

A second reason for the failure to study the gastric discharges is the lack of interest in and understanding of gastritis on the part of clinicians. This is not peculiar to Australia. The position was illuminated by a conversation with a distinguished British gastro-enterologist (Dr. "X") as follows:

> Dr. "X": "I do not believe that gastritis is a common disease."

Dr. K.: "In my experience, it is the most common cause of indigestion in those many patients with gastric symptoms in whom no gross disease (ulcer, cancer, gall-stones and appendicitis *et cetera*) can be discovered."

Dr. "X": "I gastroscope these patients, and usually see no gastritis."

Dr. K.: "A marked chronic gastritis is usually not demonstrable by inspection of the gastric mucosa (as is shown by Hale-White's 'gastrostaxis'). Even in the fresh operative specimen the disease is often unrecognizable by direct inspection. It is still less demonstrable by indirect inspection (gastroscopy)."

Dr. "X": "How then do you recognize it?"

Dr. K.: "By histological examination."

Dr. "X": "What histological criteria do you accept as proof of the disease?"

Dr. K.: "There are three—(i) infiltration of the mucosa by inflammatory elements, (ii) deformity, and (iii) destruction (going on to atrophy) of the proper or 'noble' elements in the mucosa."

Dr. "X": "I do not accept these changes as evidence of disease. Firstly, they are often found in the absence of symptoms. Secondly, similar changes, short of gross destruction, have been produced by radiotherapy, and these changes are transient and self-healing, unlike the symptoms of chronic dyspepsia."

The first objection of Dr. "X" implies that ulcer of the stomach, cancer of any organ, chronic nephritis and gall-stones are not diseases.

The second objection of Dr. "X" may be extended to organs other than the stomach. Radiotherapy can produce in all living tissues a transient inflammation. Therefore, in nature, there is no such thing as chronic inflammation.

It thus appears that the failure to recognize the importance of chronic gastritis has no reasonable foundation.

A word of warning may not be out of place. The histological examination must be thorough. Chronic gastritis is a patchy disease. It affects some parts of the stomach more than others. The pyloric antrum and the lesser curvature are usually most affected. It is patchy also in the histological sense, varying from one microscopic field to the next. Conclusions drawn from histological investigations are therefore most likely to be reliable if the whole or the greater part of the stomach is examined, as was done by such investigators as Faber and Konjetzny, and Moutier.

Aspiration biopsy has the disadvantage that it is confined to one small area, and this the least affected. It is perhaps for this reason that Ian Wood and his colleagues in Melbourne have failed to recognize the correlation between chronic gastritis and the changes in the mucosograms demonstrable by radiology.

Setälä and Sinrala (1956), in Sweden, have found, on the other hand, that "in cases with marked (radiological) changes, however, histologically detectable gastritis was always present". They investigated only those departures from the normal radiological picture which were abnormal by way of increased markings—turgor, coarseness, irregularity and thickening. If they had logically extended their observations to those variations which were abnormal by way of decreased markings, even up to the "ghost pattern", they would no doubt have discovered a greater correlation between the mucosograms and the histology.

Finally, apart from the practical importance of a proper investigation of the test meal, there are many problems of theoretical interest. My attention has been drawn to one of these by D. T. Bourke (1956). It is generally believed that the gastric mucus is secreted by the gastric epithelium, and it is well known that in chronic gastritis, when mucus abounds, goblet cells appear in the gastric mucosa, the so-called "intestinal metaplasia". But Dr. Bourke has shown that a solution having the physical qualities of mucus can be obtained by treating leucocytes with dilute alkaline solutions, which break up the cytoplasm but not the nuclei. Now it is well known that a migration of leucocytes into the stomach is a part of normal digestion and that it is increased in gastritis. Dr. Bourke suggests that this may account for some of the gastric mucus.

References.

BOURKE, D. T. (1956), personal communication.

SETÄLÄ, K., and SINRALA, U. (1956), "Roentgenologic Signs of Chronic Gastritis", *Acta radiol. scandinav.*, 45 : 199.

THE ELECTROCARDIOGRAM OF RACEHORSES: A PRELIMINARY COMMUNICATION.

By J. D. STEEL,

Department of Veterinary Medicine, Faculty of Veterinary Science, University of Sydney.

SINCE 1953 the electrocardiogram of the thoroughbred horse in training and racing has been studied intensively. An analysis of the electrocardiograms obtained from 306 horses that have contested races in Australia and New Zealand has provided a basis for defining the normal electrocardiogram and studying the changes which occurred during the racing life of these horses. Individual horses have had their electrocardiograms examined on from one to twelve occasions, depending upon opportunity and racing performance. The general plan has been to obtain an electrocardiogram as soon as possible after a horse had entered a training establishment after the yearling sales and to repeat the examination at least annually until the horse was retired or became inaccessible through sale. Included in the horses studied are winners of most of the important handicap, classic and weight-for-age races run in Sydney, Melbourne and Brisbane.

Five of the horses in the series are Australian time record holders over distances of from five to sixteen furlongs.

Electrocardiograms obtained from horses were described by Nörr (1913). Since that time a number of European, British and American workers have published studies extending the scope of the original observations. It was recognized quite early that the equine electrocardiogram was not strictly comparable with the human and canine electrocardiogram, and much effort has been expended trying to discover electrode positions—for example, French leads—which would avoid the inconvenience of placing electrodes on the limbs or make the wave form comparable to that shown by man.

In the present investigation an effort has been made to use technique, nomenclature and criteria for interpretation that follow the general principles laid down by the Criteria Committee of the New York Heart Association (1953). When necessary an attempt has been made to establish criteria that are valuable for interpreting equine electrocardiograms. On every occasion a nine-lead electrocardiogram has been obtained from each horse. The leads recorded were I, II, III, *aVR*, *aVL*, *aVF*, *CF.LA*, *CR.LA* and *CV.LA*. The letters *LA* (left apex) indicate a position on the left side of the precordium on a level with and approximately five centimetres caudal to the point of the elbow. This site of recording is roughly equivalent to position 4 in the human precordial electrocardiogram.

The essential features of the equine electrocardiogram as observed in this study are fairly similar to those described previously (see review by Lønnek and Rutqvist, 1951). The important point in the investigation has been the development of a system of interpretation which can be related usefully to the racing performance of the horses examined. "Racing performance" is a term which must be examined critically, because racing clubs devise programmes that cater for age and sex groups and for mediocre and good horses. The club handicapper may vary the weight carried, and the general quality of the horses competing varies from city to city and from season to season, depending upon the prize money offered. Despite the difficulties of a varying standard of racing and the

fact that the heart is only one of the biological factors contributing to racing performance, the electrocardiogram is a useful guide to a horse's racing potentialities. It is of little value in determining what a horse will do at a particular race meeting.

The features of the electrocardiogram as presented by the standard limb leads are used to estimate the "racing potential". Unipolar limb leads and chest leads are important in determining whether the electrocardiogram is normal.

A brief description of the normal electrocardiogram is as follows. The *P* wave duration has varied between 0·09 second and 0·17 second, with a mean of 0·1321 second. The wave form is often bizarre, and wandering of the pacemaker is common. A split, upright *P* wave isoelectric to 6 *mV* is the common finding in all leads except *aVR*, in which *P* is negative. The *P-R* interval has varied between 0·22 second and 0·66 second, with a mean of 0·3248 second. *Tp* is often readily discernible. The longest *QRS* interval observed in any one of the standard limb leads has varied between 0·09 second and 0·18 second, with a mean of 0·1216 second. Ventricular complex wave form and amplitude are variable, although in general the standard limb leads show positive deflections with prominent *R* waves. *aVR* is usually negative showing a deep *S* or *QS*, and *aVL* and *aVF* are usually predominantly positive deflections. The *C* leads are predominantly negative with deep *S* or *QS* type deflections. The *S-T* junction has shown a displacement of less than one millimetre in the limb leads and less than two millimetres in the *C* leads. *T1* is negative, *T2* diphasic ∓ or positive and *T3* positive or diphasic ∓. *TaVR* is positive or diphasic ±, *TaVL* negative and *TaVF* positive or diphasic ∓. *TCF* is negative or diphasic ∓, *TCR* diphasic ∓ or negative and *TCV* diphasic ∓ or negative. The *Q-T* interval has varied between 0·42 second and 0·62 second, with a mean of 0·5240 second. The *U* wave is most often clearly discernible in *CF.LA*. Under the conditions of obtaining the electrocardiograms the mean heart rate has been 35·90.

Data relating to age, number of races contested, total stake money won, earnings per start, mean of the *QRS* interval in each of the standard limb leads, longest *QRS* interval in any one of the standard limb leads, *P-R* interval, *P* wave duration, *Q-T* interval, *T* wave reversal, *S-T* junction shift and heart rate have been analysed to determine the product moment correlations, means, standard deviations, variances and covariances. For this an electronic high-speed universal digital computer was used.

In horses judged to have normal electrocardiagrams there is a statistically significant relationship between the *QRS* interval and the *P* wave duration and the ability to win races expressed as the total stake money won or the earnings per start. The correlation coefficients between these variables are as follows: Total stakes won/mean *QRS* interval $r_{(304)} = 0{\cdot}444$; $P < 0{\cdot}01$. Total stakes won/*P* wave duration $r_{(304)} = 0{\cdot}228$; $P < 0{\cdot}01$. Earnings per start/mean *QRS* interval $r_{(304)} = 0{\cdot}390$; $P < 0{\cdot}01$. Earnings per start/*P* wave duration $r_{(304)} = 0{\cdot}237$; $P < 0{\cdot}01$.

The mean of the *QRS* interval measured in each of the standard limb leads is slightly better than the longest *QRS* interval observed in any one of the standard limb leads as a basis for ranking the horses. Mean limb lead *QRS* intervals have varied from 0·086 second to 0·146 second with a mean of 0·1099 second. A distinct sex difference exists; the best females do not have electrocardiograms as favourable for racing as the best males.

Electrocardiograms regarded as probably abnormal or abnormal occurred in 23·85% of the horses at some time during their racing career. The abnormalities observed included atrial and ventricular extrasysfoles, atrial fibrillation, first and second degree heart block, intraventricular block, paroxysmal ventricular tachycardia, *S-T* junction shift, *T* wave changes and shortening of the *Q-T* interval. Although racing performance is adversely affected by these abnormalities, they do not necessarily preclude a particular horse from winning races.

The dominant influence of the *QRS* interval, the extent and nature of the myocardial injury, the high incidence of defects and the varying standard of racing do not allow the outright condemnation of affected animals. A *P-R* interval of 0·40 second or more is regarded as abnormal. When *T1* is flattened or positive, *TaVR* is negative and *T* in *CF*, *CR* and *CV* is positive, the electrocardiogram is regarded as abnormal. Transient changes in the direction of the *T* waves occur when the equine heart is beating rapidly. Care should be exercised in assessing the significance of *T* wave changes when the heart rate exceeds 42 per minute.

Up to the present only four horses with abnormal electrocardiograms have become available for autopsy, but in each instance there has been histological evidence of myocarditis.

A subsidiary study of the electrocardiograms of approximately 100 standard bred horses suggests that with slight modification the general principles of interpretation are applicable to pacers and trotters.

The details of this work are being prepared for publication elsewhere.

Acknowledgements.

I am indebted to the Sydney University Research Grant for the major part of the finance used for this work. I thank A. O. Ellison, Esq., for some additional financial support. I also thank Dr. P. J. Claringbold, Department of Veterinary Physiology, and Dr. J. M. Bennett, Adolph Basser Computing Laboratory, for assistance in preparing the data for analysis by the electronic digital computer.

It is a pleasure to acknowledge the cooperation of Mr. M. McCarten and the other horse trainers who made this work possible.

References.

Criteria Committee of the New York Heart Association, Inc. (1953), "Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Blood Vessels", 5th Edition, New York Heart Association, Inc., New York.

LANNEK, N., and RUTQVIST, L. (1951): "Electrocardiography in Horses: A Historical Review", *Nord. Vet.-Med.*, 3: 435.

NÖRR, J. (1913), *Z. Biol.*, 61: 197; cited by Lannek and Rutqvist (1951).

Reviews.

Modern Gynæcology with Obstetrics for Nurses. By W. E. Hector and John Howkins, M.D., F.R.C.S.; 1956. London: William Heinemann (Medical Books), Limited. 8½" × 5½", pp. 211, with illustrations. Price: 17s. 6d.

THE training of a nurse of necessity embraces a very wide field, including as it does all aspects of medical and surgical nursing. Instruction in gynæcological and obstetrical nursing forms only a part of her education, but an extremely important part, probably more so after graduation than any other portion of her training. Furthermore there is an emotional aspect to these types of patients which is absent in those of the general wards.

The authors of this admirable little book fulfil a need in presenting a subject not dealt with adequately in the ordinary text-books on nursing. Well supplemented with numerous explanatory line drawings, the text is set out in orderly fashion and, for the most part, in language readily understandable by the student nurse. The subject of gynæcology is treated very comprehensively; but, seemingly incidentally, obstetrics is disposed of in three chapters, albeit very informative, on pregnancy, abortion and normal labour respectively.

The book is no doubt intended to be complementary to the set lectures; and, although it is in parts a little too elaborate and advanced for the requirements of the average trainee, it should cater for those who wish to pursue the subject in a little more detail, as well as being useful as a reference book long after graduation. It will help the student to a better understanding of the diseases of her patients, and in so doing will make her a better nurse.

A New Psychotherapy in Schizophrenia: Relief of Frustrations by Symbolic Realization. By Marguerite Sechehaye. translated by Grace Rubin-Rabson, Ph.D.; 1956. New York and London: Grune and Stratton. 8½" × 5½", pp. 206. Price: $4.50.

IN this book, which is based on a series of lectures to the medical staff of the Bürgholzli Clinic, Miss Sechehaye describes her method of symbolic realization which proved

effective in the treatment over a period of years of a schizophrenic girl. She postulates three essential conditions for effective psychotherapy in schizophrenia: (i) adequate time, including punctuality at sessions; (ii) the belief that there is an affective life behind the patient's mask of apathy; (iii) the need to appreciate the symbolism which is represented in the bizarre symptoms by which elementary needs seek expression. This third point is claimed by Miss Sechehaye as her special contribution to the treatment of schizophrenics. We are told that Renée suffered intense emotional deprivation in her early life, and that progress in treatment began when Miss Sechehaye, having determined that apples represented to the patient maternal breasts, began to feed her with apples. The psychotherapist also acted as a mother-substitute in many other ways. The reader, who will not necessarily agree that the author's claims have been established on the basis of one case, will at least learn much of interest concerning the psychopathology of this perplexing group of mental disorders, in which, as Miss Sechehaye points out, the technique required for penetrating autism is quite different from that which is applied to manic-depressives. Chapter III, which is headed "Reactions to Flustrations" [*sic*], refers to the disturbed phases in the patient's illness.

Lectures on the Scientific Basis of Medicine. British Postgraduate Medical Federation, University of London; Volume IV, 1954-55; 1956. University of London: The Athlone Press. 8½" x 5½", pp. 406, with illustrations. Price: 37s. 6d.

A series of lectures is given each year for the British Postgraduate Medical Federation by prominent workers in many fields of scientific medicine. A selection of these lectures is published under the title "Lectures on the Scientific Basis of Medicine", and Volume IV has just appeared with 21 lectures on a wide range of subjects of fundamental importance in the development of the science of medicine. The first lecture, by Professor A. V. Hill, is entitled "Why Biophysics?" and deals with the need for more application of physics in the study of medicine and with the desirability of the development of an independent subject parallel to physiology and biochemistry. It would take too much space to consider all the subjects treated in the other lectures, but they include viruses, nucleoproteins, abnormal growth, porphyrias, blood group specificity, plasma proteins, protein malnutrition, burns, radiation injury to bone, cooling of the whole organism, fat metabolism, anatomy of the larynx and histochemistry. All the lectures, which are by prominent workers in the subjects treated, are interesting and are well written within the capacity of any physician or biological worker who has kept himself reasonably up to date. The spread of subjects is wider in this volume than in previous volumes, and the presentations in general are rather easier to follow.

The volume and indeed the whole series are strongly recommended for all physicians who wish to follow the trends of modern scientific medicine.

Proprioceptive Neuromuscular Facilitation: Patterns and Techniques. By Margaret Knott, B.S., and Dorothy E. Voss, B.Ed.; foreword by Sedgwick Mead, M.D.; 1956. New York: Hober-Harper Book. 10¼" x 7¼", pp. 146, with illustrations. Price: $5.50.

THIS book, written by two physiotherapists, has been designed as a practical guide for physiotherapists in the technique of muscle reeducation and therapeutic exercise, and it admirably fulfils its purpose. It develops the principles of the Kabat Kaiser school, in which stress is laid upon carefully graded maximum resistance throughout the entire range of motion. This is assisted by additional proprioceptive stimulation by applying stretch, by the use of synergists, and by utilizing mass movements. These general principles are discussed in Part I of the book; and they are extended in two ways: firstly, the facilitating effect of alternating resistance to isotonic contractions of antagonists and agonists; secondly, the importance of specific patterns which are spiral and diagonal.

Part II is devoted to a detailed account of the application of these principles in practice. Exercises for various regions of the body are set out. These are outlined clearly and simply; and their value is greatly enhanced by the excellent illustrations, which show clearly what the therapist is expected to do. Part III discusses evaluation of patient performance, and the planning of a treatment programme. Part IV gives a chart of patterns used for reinforcement.

This compact little book, clearly written and well illustrated, can be highly commended to all physiotherapists; and it is well worth perusal by all those interested in physical medicine.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Endogenous Uveitis", by Alan C. Woods, M.D., with illustrations by Annette Smith Burgess; 1956. Baillière, Tindall and Cox. 10" x 7", pp. 319, with 42 colour plates, 81 other illustrations, eight tables and bibliography. Price: 100s.

Intended for the student of ophthalmology "rather than for the edification of the already trained specialist".

"Varieties of Human Value", by Charles Morris; 1956. Chicago: The University of Chicago Press. 9¼" x 6", pp. 225, with illustrations and tables. Price: $5.00.

The author describes 13 possible ways to live and reports the result of an investigation among students of different nations.

"Special Lectures in Biochemistry, 1954-1955", given at the Department of Biochemistry, University College, London. London: H. K. Lewis and Company, Limited. 11" x 8½", pp. 106, with 36 illustrations. Price: 12s. 6d.

A collection of lectures put together without title page, table of contents or index.

"Textbook of Physiology and Biochemistry", by George H. Bell, B.Sc., M.D. (Glasgow), F.R.F.P.S.G., F.R.S.E., J. Norman Davidson, M.D., D.Sc. (Edin.), F.R.F.P.S.G., F.R.I.C., F.R.S.E., and Harold Scarborough, M.B., Ph.D. (Edin.), F.R.C.P.E., M.R.C.P., with a foreword by Robert C. Garry, M.B., D.Sc. (Glasgow), F.R.F.P.S.G., F.R.S.E.; Third Edition; 1956. Edinburgh and London: E. and S. Livingstone, Limited. 9½" x 6½", pp. 1080, with many illustrations. Price: 60s.

The first edition appeared in 1950 and the general arrangement of the book remains unchanged.

"A Doctor Returns", by Donald McI. Johnson; the third part of "A Publisher Presents Himself"; 1956. London: Christopher Johnson Publishers, Limited. 8½" x 5½", pp. 256. Price: 16s.

The other two parts were "A Doctor Regrets" and "Bars and Barricades".

"One Doctor in His Time", by Bethel Solomons, M.D., F.R.C.P.I., F.R.C.O.G., M.R.I.A.; 1956. London: Christopher Johnson Publishers, Limited. 8¾" x 5½", pp. 224, with illustrations. Price: 18s.

The reminiscences of the twenty-sixth master of the Rotunda Hospital, Dublin.

"Diabetes Mellitus: Handbook for Physicians", by Howard F. Root, M.D., Sc.D., F.A.C.P., and Priscilla White, M.D., Sc.D., F.A.C.P.; 1956. New York: Landsberger Medical Books, Incorporated. 8¼" x 5¼", pp. 346, with illustrations and tables. Price: $7.00.

Intended for the practitioner in his daily handling of diabetic patients.

"The Year Book of Medicine", edited by Paul B. Beeson, M.D., Carl Muschenheim, M.D., William B. Castle, M.D., Tinsley R. Harrison, M.D., Franz J. Inglefinger, M.D., and Philip K. Bondy, M.D.; 1956-1957 Year Book Series; 1956. Chicago: The Year Book Publishers, Incorporated. 8" x 5¼", pp. 744, with illustrations. Price: $6.75.

One of the Practical Medicine Series of Year Books.

"Handbook of Histology", by Karl A. Stiles, M.S., Ph.D., with an introduction by Melvin H. Knisely; Fourth Edition; 1956. New York, Toronto, London: McGraw-Hill Book Company, Incorporated. 9" x 6", pp. 253, with illustrations and tables. Price: $3.00.

The purpose of the book is to teach students to recognize tissues rapidly.

"How to Live with Your Blood Pressure", a Family Doctor Book by Baden Beatty, M.B., D.P.M.; 1956. London: The British Medical Association. 7½" x 5", pp. 142, with illustrations. Price: 8s. 6d.

Intended to provide knowledge about high blood pressure which is an antidote to fear.

The Medical Journal of Australia

SATURDAY, JANUARY 19, 1957.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE COLLEGE OF PATHOLOGISTS OF AUSTRALIA.

THE incorporation of the College of Pathologists of Australia on April 10, 1956, was the culmination of some years of activity on the part of Australian pathologists acting as a body. In 1948, at a meeting of pathologists in Brisbane, it was decided to form an Australian Association of Clinical Pathologists; provisionally Dr. A. H. Tebbutt was to be secretary and Dr. Edgar Thomson president. Later in the same year the inaugural meeting of the new association was held in Melbourne. In 1954 the name of the association was changed to the Australian Association of Pathologists, and subsequently it was decided to form the College of Pathologists of Australia. The question of incorporating the body of pathologists was first brought up by Dr. J. V. Duhig, of Brisbane; but, as Dr. Edgar Thomson pointed out in his president's address at the inaugural meeting of the college on April 30, 1956, the incorporation was for various reasons delayed, and this denied Dr. Duhig the privilege of being the first president. The college is now fully established with Dr. Edgar Thomson as president, Dr. J. W. Perry as vice-president, Dr. J. L. Holme as honorary secretary, Dr. J. R. S. Douglas as honorary treasurer, and Dr. J. I. Tonge, Dr. J. P. E. O'Brien, Dr. H. F. Bettinger, Dr. J. E. McCartney, Dr. Beryl J. Lawrence and Dr. C. A. Duncan as councillors representative of the members resident in each of the six States of Australia.

The objects of the college, as set out in its Memoranda of Association, are many. They provide for the making of contacts with other bodies and individuals, the establishment of publications, libraries, offices, museums and the like, the admission of members, and other matters necessary for the management of the college. However, most interest attaches to the first four objects, which are as follows:

> (a) To promote the study of the sciences and practice of pathology in relation to medicine; to encourage research in pathology and ancillary sciences; to bring together pathologists for their common benefit and for scientific discussions and demonstrations; and to disseminate knowledge of the principles and practice of pathology in relation to medicine by such means as may be thought fit.
>
> (b) To consider and advise as to any course of study and technical training and to diffuse any information calculated to promote and ensure the fitness of persons desirous of qualifying for membership of the College.
>
> (c) To institute and provide lectures, seminars, symposia and demonstrations upon sciences pertinent to the practice of pathology for the benefit of members of the College and to invite to and admit to such lectures, seminars, symposia and demonstrations persons who are not members of the College on such occasions and on such conditions as shall be deemed expedient by the College.
>
> (d) To consider all questions affecting the interests of the College and to promote or oppose any legislative or other measures affecting such matters concerned with pathology as are directly related to the interests of the College, or its members, as may be deemed expedient by the College.

The first of those objects sets out the broad essential basis of the college as a professional body and serves incidentally to indicate the present status of pathology. Until fairly recently, despite the passing influence of a few men of vision, pathology consisted essentially of morbid anatomy and histology, a position which was reinforced, though raised immensely in scientific status, by the development of cellular pathology under such men as Virchow. The subsequent rise of experimental pathology and the growth in complexity of clinical pathology have made the field more and more specialized and yet have strengthened the ties between the pathologist and the clinician. The days when the physician or surgeon conducted the autopsies on his own patients are virtually gone, and only some clinicians carry out even the simplest routine pathological investigations. The increasing tendency is to call on the clinical pathologist, not as a technician to "do a test", but as a consultant bringing his specialized knowledge to the problem of understanding the patient and his condition. At the same time, the pursuit of what might be called academic pathology goes on in its fundamental role of elucidating the essential nature of disease processes, encouraged not only by the scientific desire to know but also by the modern clinician's demand for a rational basis for his plan of management of a patient. Even the morbid anatomist and histologist, who a few years ago might have been regarded as working a worn-out seam, is finding new gold. As Sir Howard Florey[1] has written: "We may hope that with advances in the biological and physical sciences generally, along with the introduction of new methods such as electron microscopy, infra-red and ultra-violet micro-

[1] "Lectures on General Pathology", Melbourne University Press, 1954, page 10.

scopy, and histochemistry, and perhaps by means of techniques not yet devised, the study of morbid anatomy and particularly of histology may once again become the source of new information of first-class importance for the advancement of pathology." Another important point in assessing the status of pathology, a point that has been developed in an illuminating essay by E. S. J. King,[1] is that pathology has made a real contribution to biology. Study of the so-called abnormal has often thrown light on the nature of the "normal" and so on essential biological knowledge. Thus, if we question the right of the pathologists to make to themselves a college free from the wide embraces of the physicians' and surgeons' Royal Colleges, it may be fairly contended that pathology stands on its own ground, working out the fundamental nature of disease, moving forward to the clinician's side to share in the practice of medicine, and looking back towards the basic physical and biological sciences to contribute to as well as to draw from their store.

If the first of these four objects of the new college can be thought of as an implicit justification for its establishment, the other three are corollaries largely dependent on that establishment. The second object provides for the training and preparation of persons for membership of the college. The third encourages a programme of educational activity for members of the college and others outside the college. The fourth opens the door for medico-political activity. This is a formidable array, and places great potential power in the hands of the new college, especially when it is appreciated that membership of the College of Pathologists of Australia is, or is expected to be, a qualification registrable by the medical registration authorities in the several States of Australia. If by its influence and active participation in teaching the college can favour the development of high uniform qualifying standards for pathologists and pathology technicians throughout all States of the Commonwealth, it will achieve something of lasting value. The wider educational programme also is to be commended, and we hope that it will be used to cultivate an interest in basic pathology throughout the profession, including the ranks of the general practitioners. On the fourth object one thing needs to be said. If the college contemplates any activity in the medico-political field, we would commend to it the second paragraph of the leading article in the *British Medical Journal* of December 1, 1956. This stresses the importance in medico-political matters of having a single spearhead and points out that the British Medical Association is the only professional organization that can and does represent every branch of medicine. "Unity does not mean singing in dull unison, but it does mean singing in harmony." Close consultation is essential between the various bodies within the profession, "so that policies may be co-ordinated and action be made strong and organized by the body set up by the profession to maintain its honour and interests". To the present office-bearers of the College of Pathologists of Australia these principles will, we are sure, commend themselves. For the future, we hope that no medico-political clouds will shadow the college's path, but rather (to vary the metaphor) that it will increasingly strive to direct the light of science on to the common way as medicine moves swiftly forward.

[1] "Studies in Pathology" presented to Peter MacCallum, Melbourne University Press, 1950, page 1.

Current Comment.

EXPERIMENTAL CARDIOPNEUMOPEXY.

GRADUAL narrowing of one coronary artery is frequently followed by the development of intercoronary arterial connexions. The insufficiency is thus spread over a larger mass of heart muscle. A more desirable outcome would be the development of a new communication between the aorta and the coronary arterial system. None of the various operations devised for this purpose has proved satisfactory, though some have appeared promising for a few months only. Cardiopneumopexy is one of these operations. It has the disadvantage that, while augmenting the coronary circulation, it does so with venous blood from the pulmonary arterial system. However, it has been found by A. A. Liebow *et alii*[1] that ligation of the pulmonary artery of the dog is followed by replacement of the pulmonary arterial system by a vast ingrowth of bronchial vessels from the aorta, far beyond that required for metabolism of the lungs. In addition, transpleural arterial connexions are readily formed with adjacent vessels, such as the intercostal and pericardio-phrenic arteries. Using this knowledge, J. L. Kline, H. Stern, W. E. Bloomer and A. A. Liebow[2] ligated the pulmonary artery in the dog, and performed cardiopneumopexy at one stage. The development of collaterals was demonstrated by the use of vinylite casts. These proved to be transpleural, retrocardiac and intercoronary. Large intercoronary communications, however, developed only after interruption of the continuity of a major coronary artery. In the experimental animals this procedure was found to cause myocardial infarction. Kline and his colleagues suggest that to overcome this, anastomosis between the lung and heart may be induced in more than one site; this abolishes the necessity for large intercoronary communications. The collateral circulation arising out of cardiopneumopexy is usually well developed after five months and often well established in three months.

The advantages of cardiopneumopexy with ligation of the pulmonary artery are that arterial blood is supplied and that the lingula seems to be quite an adequate bridge for the passage of vessels to the heart. The new vascular connexions are of precapillary size and communicate with the coronary arteries and never directly with the veins. The collateral blood-flow, therefore, must have the same capillary distribution as any blood reaching the distal coronary arteries. In further studies R. A. Vidone, J. A. Kline, M. Pitel and A. A. Liebow[3] have estimated that the minimal collateral blood-flow in their animals was from 4·1% to approximately 16% of total flow into the coronary sinus, even in the absence of demonstrable cardiac ischæmia. Dye injected into the aorta proximal to the origin of the major collaterals reached levels in excess of 0·2 milligramme per 100 millilitres in the coronary sinus approximately 5·3 seconds after injection—that is, before there had been recirculation; while in control animals this level was reached after an average interval of nineteen seconds, after the dye had made the complete circuit to the left side of the heart and so to the coronary ostia. By angiographic means the circulation time from the aorta to the pulmonary veins in animals with a ligated pulmonary artery was found to be 4·2 seconds. Vidone *et alii* suggest that cardiopneumopexy may have some value in the management of transposition of the great vessels, when the pressure in the pulmonary arteries is often greater than that in the coronary vessels.

So far this operation has been performed only upon dogs. It seems reasonable to suppose that humans may benefit, too. Unfortunately, we have little evidence of the possibility of such anastomoses in humans, and to perform the operation would require a good deal of courage on the part both of the surgeon and of the patient when one

[1] *Am. J. Path.*, March, 1950, 177.
[2] *Am. J. Path.*, July-August, 1956, 663.
[3] *Am. J. Path.*, July-August, 1956, 897.

recollects the usual outcome of pulmonary artery blockage. Nevertheless, these experimental results of Liebow and his colleagues must be given due consideration by those who are interested in relieving the ischæmic heart.

LINKAGE IN HUMAN GENETICS.

J. H. RENWICK, of the Galton Laboratory, University College, London, has given a popular talk with the title "Linkage in Human Genetics" to a members' meeting of the Eugenics Society.[1] He states that early this century it was noted that the inheritance of some characters was not independent of the inheritance of some others. The concepts of linkage and linkage groups were formed, the linkage groups being later found to have their physical counterpart in the chromosomes. Linkage has to be distinguished from some other effects, especially from pleiotropy, which is due to the one gene's determining several different observable characters and from some vaguer relations, which Renwick refers to as "association", exemplified by the blood group incidence in cancer of the stomach.

In the study of genetics much work has been done on *Drosophila*, which possesses many advantages. First, it has a short life cycle and is cheap to breed; second, it possesses many readily recognizable unit characters—that is, characters dependent only on the genes at one single locus; third, it has only four chromosome pairs, which are distinguishable morphologically; fourth, some of the genes can be identified microscopically. These and other advantages have been greatly exploited by geneticists, and many refinements in the theory of genetics have resulted. Naturally, it has been hoped that this work could be applied to the study of the genetics of man, but there are some special difficulties, which may be listed in the same order as the corresponding advantages of *Drosophila*. First, the breeding of man is slow, relatively few offspring are produced by any mated pair, and the breeding is not under control of the laboratory; second, unit characters have as yet not been recognized in sufficient number—the various blood groups are the most useful of such readily recognized unit characters, unaffected by the environment—to serve as markers in the chromosomes; third, man has 24 chromosome pairs, which lessens the chances of two genes having each one locus in the same chromosome; fourth, very little is known about the morphology of the human chromosomes other than the sex chromosome pair. Two additional disabilities for the human geneticist may be noted. The same character may be produced by genes in different chromosomes; for example, some defects are carried by a gene on the sex chromosome in one pedigree but on an autosome in another. The human appears to possess a great number of modifying genes; some of these have the effect of obscuring the clear, genetical picture of brown eyes being dominant to blue, while others are believed to act in such a way as to delay the onset of symptoms in those carrying the gene for Huntingdon's chorea. But the human geneticist has some advantages. A great number of subjects are under observation throughout the world, so that a considerable number of genes giving rise to defects and disease are known. Many of these are situated on the sex chromosome, and maps have been prepared, notably by J. B. S. Haldane, showing the order of the gene loci for such defects as colour blindness, hæmophilia and pseudohypertrophic muscular atrophy. In the autosomes, progress has been slower. Renwick notes a linkage between the A B O blood group system and the "nail-patella" syndrome, characterized by defects in thumb and index, patella and pelvis. Comparatively few linkages can be regarded as well established in the autosomes. One theory places at least three gene loci for the Rhesus factor close together on an autosome, and J. Mohr[2] has reported that the Lutheran locus is linked to a gene of importance in the Lewis blood group system. Elliptocytosis and the cDE (or R_2) gene complex are linked also.

For the future, we must hope that more genes determining normal characters will be found to add to the blood group characters, tasting abilities, eye colour and hæmoglobin types which for the moment comprise almost all the useful markers available to the geneticist. At present we may mention active groups at the Galton Laboratory under Professor L. S. Penrose, at the Institute of Human Genetics in Copenhagen under Professor T. Kemp, and at the State Institute of Human Genetics and Race Biology, Upsala, but much work lies ahead. The search for unit characters and genetics generally form a particularly suitable field for clinical research in general and specialist practice.

[1] *Eugenics Rev.*, 1956, 48: 149.

[2] "A Study of Linkage in Man", Copenhagen, E. Munksgaard.

THE ADRENAL GLAND AND EXPERIMENTAL CIRRHOSIS OF THE LIVER.

NEEDLE BIOPSY of the liver is now a standard investigation measure, and by its use it is possible to give a fairly accurate prognosis in hepatitis. When incipient cirrhosis or progressive hepatitis is found, the problem arises whether cortisone is of any use. The results of cortisone therapy have so far been equivocal.

In a study of the adrenal cortex during the evolution of carbon tetrachloride cirrhosis, P. N. Wahi, H. D. Tandon and T. P. Bharadwaj[1] have produced data which may enable pathologists to indicate whether cortisone is likely to be effective or not. Cirrhosis was induced in rats by twice-weekly injections of carbon tetrachloride. Animals were killed at weekly intervals, and each week some were put aside to be killed after a further three weeks without treatment. In this way, reversibility of the cirrhotic process could be observed, for any regression that could occur did so within three weeks of ceasing the injections of carbon tetrachloride. The cirrhosis was graded into five histological categories of severity; at the same time the collagen content of the livers was estimated chemically. The authors used the term "cirrhosis" to mean any increase in collagenous connective tissue. It was found that fibrosis of the rat's liver could regress completely up to the sixth week of treatment. This took three weeks. In animals treated for longer than six weeks the changes were greater. Pseudolobulation started in the eighth week, and cirrhosis was quite severe by the ninth week. Even so, regression could occur to a certain extent after three weeks without carbon tetrachloride injections, livers in categories 4 and 5 receding to categories 1 to 3. At this stage the fibrous tissue was becoming more mature and less cellular. After the tenth week, no regression occurred, and thereafter the cirrhotic process was progressive, even when the injections of carbon tetrachloride had been stopped. During the first five weeks the adrenal cortices were hypertrophied and the reactions to stress were normal. From the sixth to the eighth week there was slight adrenal insufficiency, judging by the average ascorbic acid content, but stress could deplete the ascorbic acid content and sudanophilia almost to the normal extent. After the ninth week the adrenal was no longer able to be depleted to normal extent though the ascorbic acid values were normal. In the thirteenth and fourteenth weeks, when cirrhosis was well established and irreversible, the reactions of the adrenal to corticotrophin improved. It seems then that the reversible stage in the cirrhotic process is associated with a normally functioning adrenal, or at least one that can be induced to further activity when subjected to stress. With the onset of irreversibility, the adrenal cortex is functionally insufficient, and a return towards normal only follows the establishment of irreversible cirrhosis.

In other experiments the same authors have found that cortisone aids in the regression of cirrhosis during the phase when the process is naturally reversible. At a later stage no appreciable regression is caused. As indicated by

[1] *Arch. Path.*, September, 1956, 200 and 215.

H. Ungar, A. Laufer and D. Diengott,[1] cortisone causes diminution of cellularity of granulation tissue with more rapid maturation of scar tissue in the rat's liver. Once mature fibrous tissue has been formed, cortisone is ineffective.

If these data from rats are applicable to humans, one would expect that some improvement could take place in patients with progressive hepatitis as long as the granulation tissue remained cellular. However, once the architecture has been distorted by regenerative nodules, the only improvement that can be hoped for is to halt the formation of scar tissue between the nodules.

LEUCHÆMIA.

LARGE and important gaps remain in our understanding of leuchæmia, and there is room for many more careful studies of the data available on this disease in its various forms. Two such studies recently published[2] merit attention. Brian MacMahon and Duncan Clark set themselves to examine a representative population group by assembling data on all residents of the Borough of Brooklyn, New York, diagnosed as having leuchæmia in the period from 1943 to 1952. For this purpose they examined both hospital records and death certificates. A total of 1792 abstracts of hospital records and 1830 death certificates gave information on 1709 patients. The main Brooklyn population over the same period was used as a basis to express incidence of the various forms of leuchæmia in relation to colour, sex and age. The incidence of leuchæmia in white males and females was found to be 71·3 and 57·7 per million *per annum* respectively. Corresponding rates for the Negro population were 46·5 and 30·6. The difference between the white and Negro groups was decreased but not eliminated by standardization to allow for differences in the age distributions of the two populations; but the data in this study do not indicate whether this is a real difference in incidence or a difference "in completeness of ascertainment". Sex ratios were lower for the acute forms of the disease than for the chronic forms and, in both the acute and chronic forms, for myeloid than for lymphatic cell types. No relationship was found between sex ratio and age at diagnosis or initial white cell count. Each pathological variety of leuchæmia was found to have its own distinct age incidence. The lymphatic forms appeared to be more sharply associated with the extremes of life than were the myeloid varieties; more precisely, acute lymphatic leuchæmia appeared at a younger age than did acute myeloid leuchæmia, and the chronic lymphatic form appeared at an older average age than the chronic myeloid variety.

From their study MacMahon and Clark conclude that the various pathological subdivisions of leuchæmia differ in their relation to at least two important epidemiological variables—age and sex. This may be considered evidence of differences in ætiology between the varieties, but the position is far from clear. The incidence of leuchæmia (all types) increases with age, and this may be due to some change in constitutional susceptibility to the disease; this seems, MacMahon and Clark point out, to be a characteristic common to many types of neoplastic disorder in which many different environmental agents are suspected to be of causative significance. Differences in age trends between acute and chronic leuchæmia and between chronic myelogenous and chronic lymphatic leuchæmia are well recognized and documented from clinical experience. It appears from the present study and from another smaller study cited that similar differences exist between the individual varieties of acute leuchæmia. The fact that lymphatic leuchæmia is associated with both the extremes of age more closely than is myeloid leuchæmia raises the question whether this indicates a greater dependence of lymphatic leuchæmia on innate constitutional characteristics or changes, and of myeloid leuchæmia on more direct external environmental influences. This view is quite speculative, but MacMahon and Clark suggest that it finds some support in the fact that cases of leuchæmia attributed to whole body irradiation and to benzol are predominantly myeloid in type. Leuchæmia attributed to local irradiation of the thymus and thyroid appears to be predominantly lymphoblastic in type, but this may be a special case determined by the presence of large numbers of lymphocytes in these sites.

The other study comes from New Zealand and is concerned with the incidence and natural history of acute leuchæmia in patients over the age of fifty years. F. W. Gunz and R. F. Hough have analysed the death certificates of all patients who are stated to have died from leuchæmia in New Zealand during the five-year period from 1950 to 1954 (a total of 553), and also investigated the clinical histories of a selected group of 97 patients over the age of fifty years who died from acute leuchæmia. The analysis of the death certificates shows that 57% of the deaths occurred in patients over the age of fifty years, that more than 60% of all cases of leuchæmia were acute, and that 46% of cases of acute leuchæmia occurred in patients over the age of fifty years. As in other parts of the world, the incidence of leuchæmia in New Zealand is highest in the older age groups. Gunz and Hough state that the death rates from leuchæmia rise abruptly after the age of fifty years, and this may well be a comparatively recent phenomenon. While it has been widely accepted that chronic types of leuchæmia are mainly responsible for the increased numbers occurring in middle-aged and elderly subjects, the present figures reveal that the acute forms also play a notable part. The question is raised whether the general trend towards an older age distribution is not largely accounted for by a rise in the incidence of acute rather than of chronic leuchæmia. This remains to be investigated, but it is suggested that in any such investigation all cases of acute leuchæmia should be treated as a single group, for it does not appear profitable at present to make dogmatic distinctions between the incidence of the various types of acute leuchæmia.

The investigation of the clinical records suggests that the clinical, hæmatological and histological features of acute leuchæmia in subjects over the age of fifty years are distinctive and can be differentiated both from those of acute leuchæmia in younger patients and from those of chronic leuchæmia. The early history of the condition was found to mimic that of chronic leuchæmia in both duration and nature of symptoms, but the course of the disease differed sharply once the diagnosis had been established. The insidious onset, with its resemblance to that of chronic leuchæmia, contrasted vividly with that found in most cases of acute leuchæmia in young patients. Abnormal physical signs in patients with acute leuchæmia over the age of fifty years were few in comparison with those in members of the chronic group and probably also in children and young adults suffering from acute leuchæmia. An important way in which the group studied varied from those in the earlier phases of chronic leuchæmia and from younger patients suffering from acute leuchæmia was in the complete resistance to most forms of therapy. According to Gunz and Hough, agreement is practically unanimous among the many workers in this field that few remissions are produced in adults by the same therapeutic agents as may be highly successful in children with acute leuchæmia. Another distinctive character in the group studied was the wide variety of hæmatological and histological findings in different patients, and their lack of correlation with the length or nature of the clinical history.

Gunz and Hough believe that, because of its unusually brief clinical course after diagnosis, because of its intractability and because of the generally high degree of immaturity of the pathological leucocytes, the form of leuchæmia found in the group studied should be termed acute, whatever the duration of indefinite symptoms prior to diagnosis. They point out that we are completely ignorant of the nature of the pathological process which leads to the development of this fatal disease, and so we

[1] *Am. J. Path.*, July-August, 1956, 859.
[2] *Blood*, October, 1956.

cannot speculate whether it is the same as or differs from that responsible for the occurrence of acute leuchæmia at earlier ages. However, the frequency with which this clinical entity occurs makes it highly desirable to concentrate further research on its clinical features, on its pathological background, and especially on a means of treating it successfully.

SOME THOUGHTS ON MEDICAL EDUCATION.

AFTER a long and distinguished career as scholar, research worker, administrator and teacher in the capacity of professor of medicine, first in his native city of Amsterdam, then in China and the United States of America, I. Snapper[1] has, in a recent book entitled "Meditations on Medicine and Medical Education", drawn largely upon his special knowledge and wide global experience to give us the benefit of his considered views on a subject that has been a controversial one for the last half-century. His general observations about the future of medical education as set out in the third and last section of his book are sure to invite discussion, and perhaps criticism in some academic quarters, although his position as an acknowledged authority on such matters is in itself an assurance that his opinions will be read with lively interest and treated with due respect.

As an attractive background for his main theme of the growth of scientific medicine in the United States of America, Snapper begins by covering an unfamiliar facet of medical history with a competent and comprehensive account of the first settlement of Dutch colonists on the island of Manhattan in the mid-seventeenth century. He describes the primitive medical facilities provided for the early settlers, who had to be content with the rough and ready methods of a few unreliable barber-surgeons and self-taught midwives. It was some years before the hardy traders of New Amsterdam could count on sound medical advice given by qualified physicians thoroughly trained at the Dutch universities of Leyden or Utrecht. The quality of this training may be seen from the middle section of the book, in which Snapper summarizes the new developments in medicine and medical education so freely implemented at the University of Leyden, where the teaching of Sylvius de le Boë and his more famous successor, Hermann Boerhaave, embraced a knowledge of the basic sciences and clinical instruction at the bedside. It was a natural sequel from these innovations that the medical school acquired a European reputation, and Snapper tells how the mighty influence of Boerhaave spread first to Scotland and eventually to North America with a consequent improvement in the standard of medical practice.

When it is remembered that a medical faculty was established at Leyden in 1578, and that the Dutch tradition of medical education was translated to Edinburgh early in the eighteenth century, there is deeper significance in the appeal of Sir William Osler fifty years ago for radical reform in medical education to keep pace with the new scientific outlook. He used these words: "It is a remarkable fact in the history of medicine in England that a complete medical faculty of a university did not exist until well into the last century. Neither Oxford nor Cambridge has ever had one, nor has London, for the university of the greatest city of the world's greatest empire is a compound educational polyzoon, the units of which, like the polypoides, though highly organized and with admirable vegetative and reproductive organs, are without heart or central nervous system." Snapper gives much prominence to the views of Abraham Flexner on medical education at the beginning of this century, although Osler differed fundamentally with his pronouncements in regard to clinical studies. Yet these two men together wielded enough influence to gain (in Osler's words) "the active support of all but those whom fear of change not only perplexes but appals".

[1] "Meditations on Medicine and Medical Education: Past and Present", by I. Snapper, M.D.; 1956. New York and London: Grune and Stratton. 8¾" × 5½", pp. 144. Price: $3.75.

CLINICA CHIMICA ACTA.

A NEW JOURNAL, *Clinica Chimica Acta*, described as an "international journal of clinical chemistry", has come into being; the first three numbers have been received. There is an editorial board of fourteen persons from different countries; there is also an advisory board of twelve persons. The British members of the Editorial Board are N. F. Mcclagan, of London, and C. P. Stewart, of Edinburgh; and of the Advisory Board, R. A. McCance, of Cambridge, and A. J. P. Martin, of London. It is stated in the introduction that clinical chemistry is a world-wide affair and that from the technical point of view alone there is justification for establishing a strong international contact between the clinical chemists of every country. Apart from this, clinical values and the significance of available analytical methods need to be discussed; the indication for all kinds of estimation and their interpretation have also to be investigated. This journal apparently arose from views expressed at the First International Congress on Clinical Chemistry, held at Amsterdam in 1954; it will be published six times a year.

The journal is well produced. Articles appear, mostly in English, but also in French and German. Summaries appear in other languages, including Russian. The references are collected at the end of each contribution, but the titles of individual articles are not included, which seems a pity. Limitations of space preclude any lengthy description of contents, but the kind of subject dealt with may be seen from the following English titles in the first number: "Serum Polysaccharides in Diabetes Mellitus", "Abnormal Globulins in Some Neoplastic Diseases", "Electro-Chromograms of Human Bile", "Paper Chromatography of Urinary Amino Acids". Further information may be obtained from the Managing Editor, 31 Wright's Lane, Kensington, London.

TWO HEALTHY DEVELOPMENTS IN AUSTRALIAN MEDICINE.

Two announcements which appear elsewhere in this issue will be generally welcomed as healthy developments in Australian medicine.

The Royal Australasian College of Physicians announces the institution of a senior fellowship, the Adolph Basser Research Fellowship, for research in any branch of science associated with internal medicine. The Fellow, who must be a trained research worker, will be paid a salary at the top rate for research workers in this country, and every possible assistance is promised to ensure that he has satisfactory conditions under which to do his research work. Free from routine teaching duties, he will yet have the satisfying opportunity to "guide, train and influence" young medical graduates in research. This fellowship, applications for which close on March 15, 1957, will be a valuable addition to the limited inducements to first-rate research work in Australia if the research facilities made available measure up to the salary offered.

The establishment of a school of radiology at Royal Prince Alfred Hospital, Sydney, is a big step forward in improving the training of future radiologists. The aim of the school is to help radiologists to be "physicians as well as film-readers". The phrase is a little startling, but the point will, in general, be well taken. It has been stated that in Australia the diploma in radiology has for too long been regarded as the stamp of a specialist. In England it is only part of the way to a Fellowship of the Faculty of Radiologists and full consultant rank. In the United States of America the student of radiology has three or four years' training with experience in all branches of medicine before sitting for the appropriate examination. It is good to see this lead being followed in Australia.

Abstracts from Medical Literature.

THERAPEUTICS.

Milroy's Disease.

T. C. PANOS (*J.A.M.A.*, August 11, 1956) describes the treatment with prednisone of a patient suffering from Milroy's disease (idiopathic hereditary lymphœdema). A girl, aged eleven years, had had œdema of the legs from infancy. At the age of nine years increased swelling of the legs developed with redness, and fever occurred and recurred at intervals of four to twelve weeks. There was a family history of similar œdema. Investigations revealed no cause for the swelling. Eventually the child was treated with prednisone, 15 to 30 milligrammes daily for three weeks, and then 10 milligrammes daily in four doses. The œdema diminished greatly in three months. The dosage of prednisone was reduced to five milligrammes daily, and the remission lasted fourteen months. When prednisone therapy was discontinued, œdema recurred.

Vitamin K_1.

M. SHOSHKES AND A. J. PERELMAN (*J.A.M.A.*, July 21, 1956) discuss the use of vitamin K_1 in the treatment of hypoprothrombinæmia induced by bishydroxycoumarin ("Dicumarol"). They state that when anticoagulants are given to prevent thrombo-embolic phenomena, hæmorrhage may occur owing to dangerous depression of circulating prothrombin. The only effective antidote to this drug-induced bleeding is vitamin K_1. The authors gave this substance in doses of 50 milligrammes to 100 milligrammes intramuscularly to 20 patients. The results were variable, and the authors state that the intramuscular route is unpredictable in its results. Given by the intravenous route 50 to 100 milligrammes of vitamin K_1 produced a more consistent fall in the prothrombin time within eight to twenty-four hours.

"Diamox."

L. C. UNDERWOOD (*J.A.M.A.*, August 11, 1956) describes fatal bone marrow depression developing after treatment with acetazolamide ("Diamox"). "Diamox" (2-acetylamino-1,3,4-thiadiazole-5-sulphonamide) is a diuretic given orally in congestive heart failure. Agranulocytosis has been reported in one case in which this sulphonamide was used. The authors report another case in a patient treated with 250 milligrammes of "Diamox" daily; the drug was given for œdema with benefit for one month. There was no heart failure at the beginning of treatment, but after one month heart failure developed, and the patient died. During life, investigations showed a steady decrease in the number of leucocytes over some days, down to 225 per cubic millimetre on the day of death. The patient had a purpuric rash on admission to hospital, and oozing from nose, rectum and gums had been observed for five days before admission. The red cell count was down to 2,000,000 per cubic millimetre and the platelet count down to 15,000 per cubic millimetre. The patient was regarded as having died from agranulocytosis and thrombocytosis due to "Diamox", no other cause having been detected.

Anaphylactic Shock following Oral Administration of Penicillin.

R. C. BELL (*Lancet*, September 1, 1956) reports a case of anaphylactic reaction following the oral administration of benzathine penicillin. He states that one patient in about seven will eventually become sensitive to penicillin after repeated penicillin treatments, and draws attention to the fact that penicillin administered by any route can give rise to sensitivity. Topical applications in the form of creams are especially culpable. It is urged that the use of penicillin in any form should be restricted to occasions when there is a real clinical indication for it, and that it should not be used for trivial conditions which can be expected to heal without its use. It is suggested that individuals who have become sensitive to penicillin should carry a disk or card recording the fact.

Anticoagulant Therapy.

T. IVERSEN (*Acta. med. scandinav.*, Volume CLV, Fasc. III, 1956) discusses anticoagulant therapy with "Tromexan" and marcumar. Of 64 patients treated for so-called coronary thrombosis, 11 died in hospital and five died on discharge from hospital while still on the treatment. Four patients died within one to six days, seven died in one to five weeks, and five died in two to eight months. The report discusses mainly the action of "Tromexan" (initial dose, 900 milligrammes) and marcumar (nine milligrammes initially). It is stated that the prothrombin-proconvertin concentration was satisfactory when these two drugs were used, and that there were no untoward effects from the treatment, such as unexpected hæmorrhage. None of the deaths was attributed to the treatment.

Chemotherapy in Renal Tuberculosis.

J. K. LATTIMER AND A. L. SPIRITO (*J. Urol.*, March, 1956) review patients with renal tuberculosis who have been treated by chemotherapeutic agents over the past eight years. In this review, early cases, that is those in which there were no pyelographically demonstrable lesions, were excluded. Therefore in all the cases of this series cavitary types of lesions were present; this provided a rigorous test of the effectiveness of each regimen. One group of patients was treated with two drugs only—namely, streptomycin and PAS; this combination proved to be far more effective than streptomycin or isoniazid alone, but triple drug therapy with streptomycin, PAS and isoniazid was the most effective of all methods. The dosage was one gramme of streptomycin twice weekly, isoniazid 100 milligrammes every eight hours, and PAS five grammes every eight hours, all given continuously for one year. It was particularly noted that in this group there were no relapses in the urine culture results to positive. At the time of preparation of the report a group of 20 patients had completed one year of such treatment, with one year of follow-up. However, it is expected that some relapses will occur in future. Bed rest of a semi-ambulatory type is considered an important adjunct during the first six months, or even the whole twelve months of this treatment. This regimen has been so successful up to date that the authors have performed no nephrectomies or partial nephrectomies in the past three years. Should relapses occur later, the authors intend to precede any surgical operation by treatment for one month with isoniazid *plus* PAS, and follow up with treatment for eleven more months with the same agents. During these studies it was noted that prostatic tuberculosis responded just as well as renal tuberculosis.

The Use of C11 511 in Psychiatry.

R. COIRAULT, E. SCHULLER, M. PERRIER AND A. GUILLARD (*Presse méd.*, May 26, 1956) have carried out an investigation of the use of C11 511 (α phenyl α ethyl glutarimide—"Doriden") in psychiatry. The substance is a new non-barbituric hypnotic. The authors consider that anxiety states and disorders of personality are favourably influenced by the drug, and that it is probably a satisfactory antidote to the amphetamines. It appears useful in depressive states, because the patient awakens in a euphoric condition. It has a definite antiepileptic effect, less than that of primidone, but it is better tolerated than the latter. It seems likely to have a useful supplementary place in the treatment of neuro-psychiatric disorders bordering on epilepsy. There are indications that it is incompatible with phenobarbitone.

Early Ambulation after Myocardial Infarction.

P. BRUMMER *et alii* (*Am. Heart J.*, August, 1956) have, over a period of three years at the Medical Clinic of the University of Turku, limited the period of bed rest for patients suffering from myocardial infarction to two weeks. This regimen did not increase the rate of mortality or the incidence of complications, except perhaps the incidence of recidive myocardial infarction during the first month after the patient's discharge from hospital.

Cortisone in Pulmonary Tuberculosis.

J. B. COCHRANE *et alii* (*Brit. J. Tuberculosis & Dis. Chest*, July, 1956) have found, from a study of 19 patients, that cortisone can be safely administered to the tuberculous subject, if anti-tuberculosis chemotherapy is given concurrently. Symptomatic improvement is commonly observed. Eleven of the 19 patients were considered to have shown accelerated improvement, and the best results occurred when the lesions were relatively acute.

Hypoglycæmia and Coronary Insufficiency.

W. E. JUDSON AND W. HOLLANDER (*Am. Heart J.*, August, 1956) have found that insulin-induced hypoglycæmia failed

to precipitate *angina pectoris* in 11 patients with documented attacks of coronary arterial insufficiency. Electrocardiographic changes occurred during hypoglycæmia and were related to the reductions in the blood glucose and serum potassium concentrations. They were unlike the electrocardiographic changes observed during exercise-induced *angina pectoris*. The authors suggest that the dangers of insulin-induced hypoglycæmia in patients with coronary arterial disease may have been over-emphasized on occasion in the past.

Adrenocortical Steroids in Tuberculosis.

I. M. GOLDING, W. LESTER, JUNIOR, AND G. S. BERG (*New England J. Med.*, May 31, 1956) remark on the widespread use of the adrenocortical substances in a large variety of diseases. They point out that these drugs exert an influence on carbohydrate metabolism, reduce inflammatory reactions, keep fever and its toxic concomitants subdued, give patients a feeling of well-being, deprive the body of its ability to fight infection systemically and suppress local tissue resistance. They report four cases in which cortisone (three cases) and prednisolone (one case) appeared to have been responsible for a breakdown of pulmonary tuberculosis. They point out that in 1952 the Committee on Therapy of the American Trudeau Society issued a warning of the danger of administering cortisone to persons affected with tuberculosis (active or inactive). This committee also advised X-ray examination of the chest before, during and after hormone therapy, even in the apparent absence of tuberculosis. The authors state that patients with active or inactive tuberculosis should be protected by concomitant therapy with antimicrobial drugs and by meticulous clinical observation.

Effect of Chlorpromazine with Pentobarbital on Cerebral Hæmodynamics and Metabolism.

J. F. FAZEKAS, S. N. ALBERT AND R. W. ALMAN (*Am. J. M. Sc.*, June, 1956) discuss the combined effects of chlorpromazine and pentobarbital on cerebral hæmodynamics and metabolism. The subjects of the study were seven convalescent hospital patients ranging in age from twenty-four to forty-four years, recovering from a variety of acute illnesses. Cerebral hæmodynamics and metabolism and electroencephalograms were studied before and after the administration of relatively large doses of pentobarbital combined with moderate amounts of chlorpromazine. The characteristic electroencephalographic change after barbiturate administration tended to remain unaltered or even to improve after the administration of chlorpromazine. There was a slight diminution of cerebral blood flow and cerebral oxygen consumption after pentobarbital, but no additional interference with cerebral hæmodynamics and oxidative reactions was demonstrated when chlorpromazine was also given. Recovery from sedation induced by the combination of the two drugs was somewhat delayed. Excitation by pentobarbital in three subjects was suppressed by chlorpromazine. A combination of the two drugs may be the treatment of choice for the management of refractory hyperexcitable states.

NEUROLOGY AND PSYCHIATRY.

The Structure of Emotions Reflected in Epileptic Experiences.

DENIS WILLIAMS (*Brain*, March, 1956) discusses the structure of emotions reflected in epileptic experiences. He states that there are epileptic patients who in their attacks have elaborate coordinated movements which seem purposive, or very complex disturbances of feeling, related either to their bodies or to their environment. The disturbances which may be seen in these patients, or which may be described by them, may mimic most of the sensations and movements which occur naturally, and in any one patient the mimicry may be so close that it becomes a matter of speculation whether the disturbance is physiogenic-epileptic or psychogenic-neurotic. The author surveys 100 patients who felt an emotion as part of the epileptic experience. Ictal aggressive outbursts have been excluded. His study concerns only those with emotion and moods which, from their description, form part of the epileptic disturbance. He concludes that the emotions which arise as a result of cerebral discharges, emotions which are therefore occurring as hallucinations imposed on the patients, with no regard to external or internal environmental change, can be grouped under the headings of fear, depression, pleasure or unpleasure. The localization, as determined by electroencephalography, was found to be in one of the following areas: anterior temporal, middle temporal, posterior temporal; or it was unlocalized. In one case he describes a woman who suddenly became depressed with suicidal ideas. The episodes usually lasted for an hour or so, but had lasted for three days with fluctuations.

The Electroencephalogram and Criminal Responsibility.

R. J. ELLINGSON (*J. Forensic Med.*, July-Sept., 1956) discusses the usefulness of the electroencephalogram as an adjunctive instrument in establishing the diagnosis of functional and organic mental disease and epilepsy, or other disorders associated with defects of consciousness, particularly in relation to responsibility in criminal cases. In this regard he concludes that the electroencephalogram is of no value at the present time in the diagnosis or evaluation of functional mental disease. Abnormal electroencephalograms, especially those showing marked slow activity or focal distrubances of brain electrical function, provide supportive evidence of the existence and sometimes of the location of organic disorder of the brain. The exact nature of the disorder cannot be determined from the electroencephalogram, nor can the coexistence of mental disorder be inferred. The electroencephalogram is of greatest value in the diagnosis of epileptic disorders; especially when activation procedures are used, the exact nature of patients' seizures may be determined. The physiological conditions under which a crime is being committed may be reproduced in the laboratory and may provide strong evidence to support a plea of irresponsibility. A normal electroencephalogram cannot be considered conclusive evidence of the absence of brain disease.

Chlorpromazine and Reserpine in the Treatment of Schizophrenia.

ALBERT A. KURLAND (*Arch. Neurol. & Psychiat.*, May, 1956) reports a comparative study of chlorpromazine and reserpine in the treatment of schizophrenia. He states that 400 patients, all women, constituted a random sampling. The great majority of patients in both groups were followed for at least twelve months, and treatment lasted twelve weeks and longer. The average daily dose of chlorpromazine was from 200 to 400 milligrammes and that of reserpine was from three to six milligrammes. "Marked improvement" was shown by 9% of the chlorpromazine-treated patients and by 4% of the reserpine-treated patients.

Parkinsonian Reactions following Chlorpromazine and Reserpine Therapy.

RUPRECHT H. MAY AND GEORGE E. VOEGELE (*Arch. Neurol. & Psychiat.*, May, 1956) describe the occurrence of Parkinsonian reactions following administration of chlorpromazine and reserpine. They state that the reports of the incidence of this reaction in patients after chlorpromazine administration vary from no cases to its occurrence in all patients who are on large doses for any length of time. The authors report four cases in which Parkinsonian reactions appeared during chlorpromazine therapy and separately during reserpine medication in the same patients. These reactions disappeared shortly after cessation of medication. The drug-induced Parkinsonian reaction seems to be physiological and always reversible and to be a function of total dosage rather than a toxic symptom. It may well be a specific type of reaction of the regulatory mechanism of the central nervous system and may be therapeutically valuable.

The Surgical Treatment of Intracranial Aneurysms.

W. B. HAMBY (*Arch. Neurol. & Psychiat.*, April, 1956) reviews a series of 69 cases in which 51 patients were treated surgically with a mortality rate of 21%. In 18 cases the lesions were not treated definitely; the mortality rate was 61%. However, this group included eight patients whose physical condition was so poor that operation was never considered warranted. The time of operation after hæmorrhage is of the utmost importance. It is concluded that when feasible the ideal treatment of an intracranial aneurysm consists of occlusion of its neck by metallic clips or ligatures. Other methods constitute forced retreats from this concept. Carotid ligation is reserved for subclinoid aneurysms only.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at The Royal Women's Hospital, Melbourne, on August 1, 1956. The meeting, which was part of the hospital's centenary celebrations, took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital.

Everyday Ante-Natal Care.

DR. GEORGE SIMPSON and DR. MARGARET A. MACKIE showed four patients to illustrate everyday ante-natal care and common present-day qualifications for admission to the ante-natal wards in the hospital, the beds of which now constituted some 20% of the total obstetrical beds.

The first patient was a *multipara*, aged thirty-six years, who, in each of her previous five pregnancies, had developed hypertension in the later weeks. She was admitted to hospital because at her routine ante-natal visit a few days previously, at thirty-five weeks, her blood pressure had risen from 140/80 to 160/105. There was no abnormal weight increase or albuminuria. She was admitted to hospital for assessment and observation, and already with bed rest her blood pressure had fallen. She would probably be discharged with instructions to carry out the hospital routine at home, and be checked twice weekly in the ante-natal clinic. If her condition remained satisfactory, labour would be induced at thirty-eight or thirty-nine weeks, or earlier if her blood pressure should rise again.

The second patient was a girl, aged nineteen years, with a twin pregnancy at thirty-two weeks. Patients with twins were admitted if there was any evidence of toxæmia or other complications, or if the domestic set-up was unsatisfactory. Hospitalization had lessened the severity of complications and the likelihood of premature birth. The patient was a single girl from a home, and she had been admitted to hospital for short periods twice previously for anæmia requiring transfusion. The present admission was because of excessive weight gain. It was obvious that she had been careless regarding diet and anti-anæmic treatment while not under hospital supervision. It was pointed out that admission to hospital for weight control by diet was particularly useful in the case of New Australian patients. A few days' demonstration of the diet was of much more value than diet charts and instructions, even when given in the patient's own language.

The third patient, who had severe anæmia of pregnancy, was a young high-coloured Italian girl who could speak no English. She was thirty-eight weeks pregnant. At her first visit the hæmoglobin value was 80%, which was accepted as the desirable level to maintain during pregnancy. At thirty weeks the value found at routine hæmoglobin estimation dropped to 60%. Treatment was prescribed, but probably was not carried out, and the next reading was again 60%. Intramuscular iron therapy was then given, but at her last ante-natal visit there was still no improvement. As she was now only two weeks from maturity, she was admitted to hospital for blood transfusion. The patient was shown to illustrate the deception of "make up" and the necessity for routine hæmoglobin estimation in pregnancy.

The fourth patient was a girl, aged twenty-three years, with rheumatic carditis. In her one previous pregnancy she had been found to have mitral stenosis. At twenty-two weeks she had developed congestive cardiac failure, and had been treated in hospital for two weeks. Again at thirty-four weeks she had required admission to hospital and had remained in hospital until delivered at term. After her confinement she had undergone valvotomy at the Royal Melbourne Hospital in 1955. During the present pregnancy she had been perfectly well, but at a routine ante-natal visit a short time before the meeting she was found to have gained six pounds in weight in two weeks. That could have indicated fluid retention of cardiac origin or incipient toxæmia. She was admitted to hospital for weight control, and in one week, receiving a 1724 Calorie diet and resting in bed, she had lost three pounds. Heart function and efficiency were normal, and she was to be discharged from hospital shortly. Normal labour was anticipated. It was stated that patients with cardiac conditions were generally admitted to hospital at about thirty-four weeks for observation, rest and assessment. Labour at full term was desirable.

Acute Mastitis.

DR. JAMES SMIBERT discussed the results of treatment of acute mastitis, classifying them according to the initial treatment instituted and the result obtained. The series covered the period from 1953 to 1956. In eight cases the initial treatment was unknown, and in all the abscesses were incised. Pathological examination showed that four of the infecting organisms were penicillin-resistant, in three cases the finding was "unsatisfactory", and in one case the organism was penicillin-sensitive. Of 33 patients treated with penicillin, or sulphonamide drugs, or both, the condition resolved in 17, and 16 abscesses were incised; in 12 of these 16 cases the infecting organism was penicillin-resistant, and in four the finding was "unsatisfactory". One patient was treated with "Aureomycin" and 42 were treated with "Terramycin"; resolution occurred in 42 of these cases, and in one in which "Terramycin" therapy was started forty-eight hours after the onset, incision was required. Dr. Smibert said that the three common sites of puerperal infection were the birth canal, the urinary tract and the breast. In infections of the birth canal and the urinary tract, the infecting organism was easily grown on culture and tested for sensitivity; most such infections would respond to penicillin, sulphonamides, or a combination of both, and treatment with those agents should be administered pending the results of sensitivity tests. In breast infections, the infecting organism could not be recovered until an abscess had formed; that was too late. For all practical purposes the infecting organism was always *Staphylococcus pyogenes*. An appropriate antibiotic had to be given early; in 1956 that meant one of the tetracycline series, not penicillin, to which about 50% of staphylococci were resistant. Dr. Smibert drew the attention of those present to the fact that "Aureomycin", "Terramycin" and "Achromycin" might be prescribed as pharmaceutical benefits for staphylococcal infections that did not respond to penicillin.

Recurrent Abortion.

DR. W. J. RAWLINGS gave a demonstration relating to recurrent abortion. The demonstration consisted mainly of graphs on the urinary excretion of pregnanediol as an indication of the metabolism of progesterone. Selected graphs were shown from a series of 293 patients on whom 7700 pregnanediol urinary excretion tests had been performed. Tests on twenty-four-hour specimens were performed at weekly intervals, when possible, from the commencement to the thirty-fifth week of pregnancy. For purposes of basic data some tests were commenced even when the membranes had ruptured or when the case clinically was one of inevitable abortion. The following graphs were displayed:

1. A normal curve. Dr. Rawlings said that the excretion graph was parallel to the average normal curve; the latter was a better guide than the earlier curve of Venning.

2. Typical abortion curves. These were divided into the following four types: (*a*) The type in which a high pregnanediol value suddenly steadily fell to the non-pregnant level, abortion following. (*b*) Cases of "brown loss" *per vaginam* with a very low pregnanediol value, followed by "red loss" *per vaginam* and abortion. (*c*) Cases in which "brown" to "red" loss occurred *per vaginam* and the pregnanediol level could not be raised by ethisterone or progesterone, abortion following. (*d*) Cases in which, at a later period, twenty to thirty-five weeks, after threatened abortion, the level of pregnanediol was raised by ethisterone and then later gradually fell, death of the *fœtus in utero* and abortion following.

3. Graphs in which threatened abortion was prevented, and the curve was raised to between the normal average and the clinical critical level by the exhibition of ethisterone or progesterone. In those instances small quantities of ethisterone (20 to 50 milligrammes per day) easily maintained the level, and pregnancy continued to term.

4. Cases more difficult to maintain in the "safe" zone, the patients requiring in some instances 100 to 200 milligrammes of ethisterone per day; in a few instances this had to be supplemented by progesterone injections of 20 to 100 milligrammes per day. One patient in the fourth group showed a positive Aschheim-Zondek reaction at six weeks of pregnancy, it having been necessary to administer up to 200 milligrammes of ethisterone per day to maintain her near the critical clinical level. At thirty-seven weeks of pregnancy, because of the small size of the uterus, a consultation was held, and after artificial rupture of membranes, followed by Cæsarean section, a living baby weighing two

pounds ten ounces was delivered. Dr. Rawlings said that that was a very good example of deficient placentation.

5. Graphs of uterine cramps in relation to pregnanediol excretion. One simple graph showed a pronounced fall in excretion concurrent with abdominal uterine pains during the collection of the twenty-four-hour urinary specimen. Other graphs showed recurrent falls associated with repeated episodes of uterine cramps, in which condition the patient felt the enlarged abdominal uterus tighten and harden, and had the feeling of the vulval passage opening up or of a desire to bear down. By the ingestion of ethisterone, 25 milligrammes, at the time patients obtained relief of their cramps and cessation of contractions, which did not proceed to dilatation of the cervix.

6. Graphs of successive pregnancies in the same patient, showing a pronounced similarity of pattern. In one particular case four previous abortions had occurred. In 1955 the pregnanediol level was raised and maintained by ethisterone and the pregnancy was brought to a successful conclusion. In 1956 ethisterone was withheld, and the pregnanediol level fell till death of the *fœtus in utero* and abortion occurred at twenty weeks—the usual time.

7. Trophoblastic failure, in which the pregnanediol level was high in the satisfactory pregnancy range. The test for pregnancy, which had previously given positive results, now became doubtful (positive in the rat, negative in the toad), and later the results in both rat and toad became negative.

Dr. Rawlings presented an analysis of the results obtained in 170 cases in which pregnanediol tests had been made; the analysis was divided into three columns, as follows: (i) patients with normal pregnanediol levels and untreated, 62% of whom went to term; (ii) patients with low pregnanediol levels and untreated, only 36% of whose pregnancies were successful; (iii) patients with low pregnanediol levels and treated adequately with ethisterone or progesterone, 70% of whose pregnancies were successful. The investigation showed that 34% of abortions were due to deficient progesterone metabolism, and therefore at least 34% of threatened abortions could be prevented. The other main factors of rapidly falling blood hæmoglobin level, post-coital bleeding and emotional factors were discussed.

Sims's Post-Coital Compatibility Test.

DR. J. W. JOHNSTONE gave a demonstration of Sims's post-coital compatibility test illustrated by sperm behaviour in the different qualities of cervical mucus. He said that credit for the test should go, rather than to Max Huhner of more recent years, to J. Marion Sims, well known for his work on fistulæ, and for his vaginal speculum and gynæcological posture, who had described the essentials in 1868. *The Medical Times and Gazette* of the period described Sims's procedure as "this dabbing in the vagina with speculum and syringe—incompatible with decency and self-respect". Recent years had seen a return to popularity of post-coital examination of the sperms in their natural environment, the cervical mucus. The test could be performed in general practice and should be regarded as complementary to the seminal analysis, although the latter added nothing when a fair saturation of vigorous sperms could be seen in good quality cervical mucus. The test had the advantages of requiring little or no cooperatiaon on the part of the male, but confirmed his ability to perform the act. Transport was easy; the examination could be repeated, and it suffered no religious drawbacks. It was best performed in the mid-cycle two or three hours after intercourse; but the time interval after coitus was not very important. A favourable result could be expected after ten or twelve hours, which was an advantage for country patients.

Dr. Johnstone went on to say that as the sperms permeated the cervical mucus, the less vigorous kept falling out against the resistance, so that it appeared to exert a chemotactic attraction for them. The plug acted as a sieve as well as a reservoir, from which there was a continuous ascent over perhaps two days, only one in many thousands of sperms ever reaching the outer part of the Fallopian tube. Fruitful coitus should precede ovulation, so that the egg could be discharged into the most favourable environment. The vaginal acidity activated, but exhausted, the sperms, so that they were all dead within an hour in the vaginal fornices. The cervical mucus, being difficult to aspirate, required a narrow syringe, strong suction being maintained as it was withdrawn. The cervical mucus underwent cyclical changes, being more abundant and receptive to sperms at the end of the œstrogenic proliferative phase, when it appeared like egg albumen. At that time the water and salt concentration was such that if the mucus was simply allowed to dry on a slide, the typical crystallization in fern-like manner was easily evident. That was demonstrated under the microscope.

Dr. Johnstone further said that in performing the test the aspirated mucus should be discharged in a drop onto a slide and covered with a slip, and was best examined under rather low power. Consideration should then be given to two factors, female and male. The canal should be filled with an abundant quantity of mucus, in favourable cases protruding in a cascade into the seminal pool. Contrary to accepted opinions, some erosions, particularly of the hormonic type in *nulliparæ*, assisted in the exteriorization of mucus, and were favourable for the attraction of sperms. A narrow or pinhole os was likely to hinder drainage and produce a "dry tap", or to be associated with tenacious "chewing-gum" mucus of poor quality. The mucus should be clear water-white, rather than opaque paper-white, or worse still, yellow-green and purulent, which indicated cervicitis and infective erosions. The microscopic appearance could be correlated with the cellular content on microscopic examination. Viscosity was an important property; the mucus, instead of being passed from one slide to another in a blob, should be capable of being drawn out into long threads of almost endless length. That was the important and favourable property known as *Spinnbarkeit*. On the male side, attention should be given first to general sperm density. The practitioner, used to his own microscope, would cover a wider field and obtain more information from a rather low power and by moving the slide about. Not much information would be obtained about sperm morphology, but the general percentage of sperms showing life or motility could be estimated, just as was done in semen analysis. Most important of all was what might be called vitality or quality of movement, indicated by speed, a darting movement, and quick forward progression, as opposed to a more stationary vibration and bunting oscillations. The seminal analysis gave a list of figures by which the male could be assessed on a ladder of fertility, although there could be fallacies in interpreting those mathematics too rigidly. Putting all the factors together in Sims's compatibility test, by allotting four *plus* signs for the male and four for the female, and remembering that one side conditioned the other, Dr. Johnstone thought it was possible to give expression on paper to something which could only be qualitative and personal.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

MEDICAL DEGREES AT THE UNIVERSITY OF SYDNEY.[1]

[Although the Sydney Medical School did not open until 1883 the Act of Incorporation empowered the University to grant degrees in medicine as well as in arts and law. The conditions which candidates must fulfil are set out in the *New Medical Gazette* of December, 1870.]

A professor of chemistry has been appointed by the Senate in connection with the Faculty of Medicine and associated with him is a board of examiners. The professor of chemistry is John Smith, M.D., who is also Dean of the Faculty. The other examiners are W. G. Alleyne, M.D. (Cambridge): Edward Bedford: G. Bennett, M.D. (Glasgow): Sprott Boyd, M.D. (Edinburgh): John Macfarlane, M.D. (Glasgow): Charles Nathan: Alfred Roberts. Candidates for the degree of M.B. must lodge with the Registrar of the University satisfactory certificates of having taken the degree of B.A. or some equivalent degree in this or in other Universities as permitted by the Senate equivalent to that of the Sydney University: but if he has not already obtained the degree of B.A. he must undergo a similar examination to that required for the degree of B.A. before he be admitted to examination for the degree of M.B. It is however in the power of the Senate to dispense with the examination in the case of candidates who have been in bona fide medical

[1] From the original in the Mitchell Library, Sydney.

or surgical practice for not less than ten years. The candidate must also furnish evidence that he is of good fame and character, that he is not under twenty-one years of age, and that he has diligently pursued a course of medical studies extending over a period of four years at some medical school approved by the Senate. The certificate must show that he has attended the following eight classes each for a course of six months viz. Anatomy, Practical Anatomy, Physiology, Chemistry, Materia Medica, Surgery, Practice of Medicine, Midwifery: and the following five classes for a course of three months viz.: Botany, Practical Chemistry, Medical Jurisprudence, Clinical Medicine and Clinical Surgery: also that he has attended for eighteen months the medical and surgical practice of a hospital containing not fewer than eight beds, and that he has been for six months engaged in compounding and dispensing medicines. The fee for the examination of M.B. is ten pounds. The degree of M.D. cannot be conferred until two years after the granting of the M.B. degree. The candidate must prepare a thesis in Latin or English on a medical subject to be selected by himself and pay a fee of ten pounds. The degree of Doctor of Medicine has been conferred on the following gentlemen: In the year 1868 on C. F. Goldsboro: in the present year on James Houison and Patrick Smith. The degree of M.B. has been granted to the following gentlemen: In the year 1867 to Patrick Smith and during the present year to F. Lloyd, G. Moore, C. Stewart and Richard T. Jones.

Correspondence.

NORTH QUEENSLAND MEDICAL CONFERENCE, 1958.

SIR: The closing meeting of the last North Queensland Medical Conference, held at Cairns in May, 1956, decided that the next North Queensland Medical Conference would be held in Mackay in 1958. The Queensland Branch of the British Medical Association has allocated the week from Monday, September 22, to Friday, September 29, 1958, for the conference, and our committee would appreciate it if you bring these dates to the notice of your readers.

The previous conferences, at Townsville in 1954 and in Cairns in 1956, have been outstandingly successful from the clinical and social viewpoints, and have allowed many less fortunate members of the profession to see the tropical north at its best and to understand its peculiar medical problems. We think that Mackay will not fall below the high standards set by the other tropical towns, but trust that many southern visitors will attend to swell our ranks, and bring their cosmopolitan opinions to our otherwise parochial discussions.

Yours, etc.,

IAN CHENOWETH,
Secretary, North Queensland Medical Conference (Mackay).

Sydney Street,
Mackay,
North Queensland.
December 18, 1956.

ACTIVE IMMUNIZATION AGAINST TETANUS.

SIR: The board of management and the honorary medical staff of the Royal Alexandra Hospital for Children have given consideration to the subject of active immunization against tetanus.

Six to eight cases of tetanus are admitted annually to this hospital, and many are treated in other metropolitan and country centres. The mortality in this hospital is approximately 40%, and in recent years we have found tetanus to be more common than diphtheria as a cause of death in childhood. Tetanus frequently follows injuries which have been considered so trivial as not to warrant a visit to the hospital or local practitioner, with the result that antitetanus serum has not been given.

Active immunization against tetanus is now easy and safe. Minor allergic reactions to toxoid do occasionally occur, but are rarely serious; triple antigen provides protection against tetanus, diphtheria and pertussis; and tetanus toxoid alone, or preparations which combine diphtheria and tetanus toxoids, are suitable for use when immunization against diphtheria and/or pertussis has previously been carried out. Moreover, active immunization eliminates the need for the administration of foreign serum, which carries the danger of severe hypersensitivity reactions, and which is often administered in dosage too small to provide adequate prophylaxis.

There is ample evidence to support universal active immunization. Coneybeare and Logan (1951) attribute the lower incidence of the disease in the middle years of life to the active immunization of service personnel. After a comprehensive review of the epidemiology of tetanus in Queensland, recently published in this journal, D. W. Johnson concludes that "widespread active immunization is the only way to reduce the incidence of tetanus".

The Royal Alexandra Hospital for Children advocates, as a matter of public health policy, the active immunization against tetanus of all children who have not previously received this protection.

Yours, etc.,

LINDSAY DEY,
President, Royal Alexandra Hospital for Children.

Camperdown,
New South Wales,
December 19, 1956.

NOMENCLATURE OF THE BLOOD CLOTTING FACTORS.

SIR: I should like to draw your attention and invite cooperation in the following problem. Most workers, whether they are specialists or have a general professional interest, are very concerned with nomenclature of physiological and pathological conditions, and their underlying causes. In a rapidly expanding field, like that of blood coagulation and its disorders, workers found it desirable not only to describe a phenomenon, but thought it justified in giving it a name. It has become apparent that in several instances the same condition or factor associated with a particular condition has been given different names. This has created an undesirable situation, and "coagulationists" have been accused of using a code language difficult to follow by others who have to be familiar with the progress of blood clotting for diagnosis or treatment of their patients, or for students of hæmatology. In an endeavour to solve this problem, an "International Committee for the Standardization of the Nomenclature of the Blood Clotting Factors" has been founded with the aim to suggest a generally acceptable scheme for naming established blood clotting factors, and for the purpose of studying new phenomena which are thought to be associated with unrecognized blood clotting factors. In this way it is hoped that unification of nomenclature will be achieved, and therefore the complex field of blood coagulation will be made more easily comprehensible.

It will be appreciated if you and your readers would submit any suggestions related to this subject to the undersigned, or directly to the present chairman, Dr. Irving S. Wright, the New York Hospital, 525 East Sixty-Eighth Street, New York 21.

Yours, etc.,

P. FANTL.

Baker Medical Research Institute and Alfred Hospital Clinical Research Unit,
Commercial Road,
Melbourne, S.1.
November 30, 1956.

GOUT, RHEUMATISM AND INFECTION FROM HIPPOCRATES TO HENCH.

SIR: Since I had the pleasure of hearing Dr. Michael Kelly deliver his paper "Gout, Rheumatism and Infection from Hippocrates to Hench", which has now been published (M. J. AUSTRALIA, December 15, 1956, page 877), the following facts have come to my attention. I think that they might be of interest when taken in conjunction with certain parts of the paper.

Dr. Kelly mentioned the concept of the "four humours" in the causation of disease. In the preface of "Blood Cells and Plasma Proteins" (1953, page ix), edited by James L. Tullis, the historical researches by Fahraeus in 1921 on the origin of this concept are mentioned. Unfortunately I have not been able to locate Fahraeus's original paper, but the results of his investigations are as follows. Observers noted that when clotted blood from a healthy person stood for a while, the clot retracted and clear serum appeared. This clear

serum was the "clear bile or yellow bile". We thus have the first two "humours", "blood" and "clear bile". But when the blood from patients suffering from certain diseases was allowed to stand, they observed that a "buffy coat" formed on the top of it. This we know today to be fibrin, and it is an indication of rapid sedimentation; to the ancients this was "phlegm", the third "humour". They realized that it was of the same nature as the phlegm of fibrinous discharges. The fourth "humour", the "black bile", was simply altered blood. In fact it is only a little over a century since men began to realize the true nature of the "black bile" seen in hæmatemesis and melæna.

Here we have an example of something which is by no means unique in the history of scientific thought, and which shows how far one can be led astray by pushing one's conclusions to extremes. On the basis of observations which were themselves perfectly accurate, a complete system of medicine was built up and a false hypothesis was established and held for many centuries. At the same time, the observations themselves continued to be of practical value, particularly in diagnosis and prognosis.

Yours, etc.,

4 Moorhouse Street,
East Camberwell,
Victoria.
December 21, 1956.

MURRAY L. VERSO.

FAT EMBOLISM.

SIR: The editorial on fat embolism in your issue of December 15 I found most interesting. I once undertook a small research on the size of fat particles in the thoracic duct lymph in a few domestic animals and, as might be expected from theoretical considerations, found that the maximal diameter was well below capillary size. Obviously there is in the epithelium of the absorbing villus some mechanism for standardizing the dimensions of the fat droplets. In trauma, I take it, unstandardized fat particles from bone marrow or adipose deposit enter the tissue fluid and are drained away by lymphatic vessels, eventually reaching the blood circulation through the thoracic duct. The time interval between the trauma and the onset of fat embolism, two days mostly, fits in with the rate of lymph flow in the unmassaged limb.

Yours, etc.,

The Hall,
Kangaroo Ground,
Victoria.
December 19, 1956.

W. A. OSBORNE.

Post-Graduate Work.

SCHOOL OF RADIOLOGY AT ROYAL PRINCE ALFRED HOSPITAL, SYDNEY.

A SCHOOL OF RADIOLOGY is to be established at Royal Prince Alfred Hospital, Sydney, commencing on March 1, 1957. The school will provide training in radiodiagnosis and radiotherapy in conjunction with the courses conducted by the Post-Graduate Committee in Medicine in the University of Sydney for the diplomata of the University of Sydney and the College of Radiologists of Australasia. Enrolment in the school will be for two years.

Training will include the following: (i) Radiodiagnosis: general pathology, histopathology, anatomy, physics, electrotechnology. (ii) General: medical and surgical rounds, seminars, clinico-pathological conferences, thoracic unit clinics, gastro-enterological clinics. (iii) Radiology: general, thoracic, gastro-enterology, pædiatrics, obstetrics, gynæcology, neurosurgery, cardiology, orthopædics, urology. (iv) Practical: radiography, film processing, gastro-intestinal examinations, urological examinations, tomography, and other specialized examinations.

An extensive film and 35-millimetre slide library is available. Professor E. Ford, Dean of the Faculty of Medicine, has made the library in the New Medical School available to members of the school, and Professor F. R. Margarey, Professor of Pathology, has also made the pathology museum available.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED DECEMBER 22, 1956.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	..	..	..	..	..	..	..	..
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	1	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	1	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	7	2(1)	2	..	..	..	1	..	12
Diphtheria	2(2)	..	..	..	1(1)	..	..	..	3
Dysentery (Bacillary)	..	3(3)	5(3)	..	2(2)	..	..	..	10
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	39(18)	21(9)	..	6	1(1)	5	3	..	75
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	2	..	..	..	..	..	2
Malaria	..	..	1(1)	..	..	..	..	..	1
Meningococcal Infection	2(1)	3(2)	..	1(1)	..	..	..	..	6
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	1(1)	..	..	..	..	..	..	1	1
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	1(1)	..	1	1(1)	..	..	..	3
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	16(12)	..	145(118)	2(2)	..	..	..	163
Salmonella Infection	..	..	..	..	1(1)	..	..	..	1
Scarlet Fever	5(5)	4(3)	9(2)	11(5)	1(1)	2	..	..	32
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1	..	..	..	..	..	1
Trachoma	..	..	..	..	1(1)	..	..	..	1
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	37(23)	7(3)	9(6)	6(6)	6(6)	3	2	1	71
Typhoid Fever	2(2)	..	..	..	..	..	..	..	2
Typhus (Flea-, Mite- and Tick-borne)	1	..	..	1(1)	..	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Radiodiagnosis.—There are appointments for five registrars in diagnostic radiology. There will be two vacancies on March 1, 1957. There will be vacancies for graduates, non-salaried. These graduates will be eligible for appointment as registrars as they fall vacant. Provision will be made for attendances at all lectures conducted by the Post-Graduate Committee in Medicine, which cover the requirements set by the University of Sydney and the College of Radiologists of Australasia.

Radiotherapy.—There are appointments for two registrars in radiotherapy. There will be one vacancy on March 1, 1957. Training will include the following: (i) General: pathology, histopathology, physics, anatomy, electrotechnology, medical and surgical rounds. (ii) Radiotherapy: superficial therapy, deep X-ray therapy, supervoltage therapy, radium, radon, isotopes.

Further information may be obtained from Dr. Alan R. Colwell, Director of Radiological Services, Royal Prince Alfred Hospital, Camperdown, New South Wales.

The Royal Australasian College of Physicians.

THE ADOLPH BASSER RESEARCH FELLOWSHIP.

THE Adolph Basser Research Fellowship has been instituted by The Royal Australasian College of Physicians for research in any branch of science associated with internal medicine.

The conditions of appointment are as follows: (i) The title of the person appointed will be the Adolph Basser Research Fellow of The Royal Australasian College of Physicians. (ii) The term of the appointment will be for five years with a possible renewal for a further term. (iii) The Fellow must be a trained research worker in a field related to the problems of clinical medicine. (iv) Except with the consent of the Council of The Royal Australasian College of Physicians, the Fellow will not be allowed to engage in private practice or tuition, or any other profession or business. (v) The tenure of office will be subject to the following limitations: (*a*) the Council has the power to terminate the Fellowship on the grounds of misconduct; (*b*) the Council has the power to terminate the Fellowship, without cause shown, if for any reason the Fellow should, in the opinion of Council, become incapable of continuing his research in a satisfactory manner. (vi) The Fellow will be paid a salary at the rate of £A3750 *per annum*. In addition the Council of The Royal Australasian College of Physicians will, for the term of the Fellowship, pay a yearly sum equal to 10% of the Fellow's salary by way of contribution to a superannuation provision, the Fellow's own contribution being at the rate of 5% yearly of his salary. The Fellow is expected to enter upon his research by a date to be arranged between him and the Council of The Royal Australasian College of Physicians and the salary shall commence from that date or, in the case of an appointee from overseas, shall commence from the date of embarkation at the overseas port, provided that the appointee is proceeding direct to Australia to take up his appointment. (vii) The research programme should show promise of a definite contribution to knowledge in clinical medicine. (viii) The research must be done in Australia or New Zealand. The place in which the work will be done will depend to some extent on the nature of the research, and the candidate is required to set forth his requirements as to space and his wishes as to locality. The Council of The Royal Australasian College of Physicians will be responsible for final arrangements in this regard and will do all in its power to establish the Fellow in a research department or institute where he can fulfil the requirements set down in these conditions. (ix) A sum of money will be granted for technical help, equipment and overhead expenses for the first year; but this will be subject to review in the light of requirements of the research. (x) There are no routine teaching duties associated with the appointment, but it is anticipated that the Fellow will give occasional lectures in his special field to appropriate groups. He should also be able to guide, train and influence young medical graduates in research. (xi) The Fellow will be entitled to four weeks' recreational leave *per annum*. During the five-year term of his Fellowship the Fellow will be entitled to a total of three months' sick leave on full pay and a further total of three months' sick leave on half-pay. (xii) The successful applicant, prior to appointment, will be required to satisfy a medical examiner appointed by the Council as to his good health. (xiii) Should he be elected to a House of Parliament, either Federal or State, the Fellow will be required to resign his Fellowship as from date of election. (xiv) The Fellow will be required to prepare a statement on the work accomplished together with a list of publications for submission to the Council by the first day of October in each year. He also will be required in any publication to make due acknowledgement that the work has been carried out as the Adolph Basser Research Fellow of The Royal Australasian College of Physicians. (xv) Ten reprints of any publication will be furnished to the Council by the Fellow. (xvi) Any apparatus purchased for the research activities of the Fellow shall become the property of The Royal Australasian College of Physicians.

Applications, which close on March 15, 1957, should be addressed to the Honorary Secretary, The Royal Australasian College of Physicians, 145 Macquarie Street, Sydney, from whom details may be obtained of the form in which applications should be submitted.

Deaths.

THE following deaths have been announced:

McCAFFERTY.—George Henry McCafferty, on January 3, 1957, at Brisbane.

BARRY.—Alfred Broughton Barry, on January 9, 1957, at Sydney.

Diary for the Month.

JAN. 23.—Victorian Branch, B.M.A.: Council Meeting.
JAN. 25.—Queensland Branch, B.M.A.: Council Meeting.
FEB. 5.—New South Wales Branch, B.M.A.: Organization and Science Committee.
FEB. 6.—Western Australian Branch, B.M.A.: Branch Council.
FEB. 6.—Victorian Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 *per annum* within America and foreign countries, payable in advance.